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OCULOGYRIC CRISES IN CHRONIC EPIDEMIC ENCEPHALITIS.

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Introduction.

Chronic epidemic encephalitis has from the first been associated with manifestations of a bizarre and striking character. The majority of these phenomena have been of a hyperkinetic type and include choreic, athetoid and myoclonic movements, motor tics of all descriptions, generalized convulsions, paradoxical activity, respiratory crises, and lastly, the tonic eye spasms termed by the French *crises oculogyres*. These have been recognized for little more than three years, and it is doubtful if they occurred before 1923.

There can be little doubt that certain of these hyperkinetic manifestations, such as the myoclonic and respiratory phenomena, are on the wane, and none at all that the incidence of oculogyric crises is increasing. Our series of 23 cases is taken from a total number of 136 encephalitics, all of whom are, or have been, patients in West Park Mental Hospital or the Manor Institution for mental defectives. This constitutes an approximate proportion of 17 per cent. It is a matter of some difficulty to obtain accurate histories of the onset of the attacks in all cases, but as far as can be ascertained in only 6 of the 23 cases did the crises occur before 1926. On the other hand, 5 out of the last 9 encephalitics admitted to West Park have been thus affected. The earliest date of origin in our series appears to be 1923; another case started fairly definitely in the autumn of 1924. There is evidently no relation

between oculogyric crises and any special epidemic, as the dates of the primary attacks of encephalitis that were followed by crises include every year from 1919 to 1925. Again, it is impossible to foretell how long after the primary illness the onset of this phenomenon may be expected, as in two of our cases the attacks commenced within six months, while several remained free for six years, and in one there is no evidence of the crises beginning until eight years after she first became ill. In all our cases the onset of Parkinsonism preceded that of the crises, but periods varying from a month or two to five or six years separated the onset of the two syndromes. The nature of the primary attack likewise offers no criterion as to the possibility of the development of ocular spasms, and our series includes all varieties of primary illness, acute and gradual, mild and severe. This lack of relationship helps us little in forming an hypothesis of the origin of these attacks, except that it tends to emphasize the progressive nature of the disease and the unimportance of the nature of the primary attack and of the epidemic on the resulting sequelæ. The increasing prevalence of this distressing manifestation is another problem that at present must be left unsolved.

No theory appears to us sufficiently reasonable to put forward, and we can but wait for fresh light to be thrown upon the subject by means of larger experience and further investigations. The suggestions as to the pathological basis of these manifestations which we are bringing forward in this paper are evolved from clinical considerations, combined with certain facts in the physiological anatomy of the ocular mechanisms. These support our view that the lesion accountable for the crises does not lie in the lower centres for conjugate deviation, but in the associational centres or paths leading to them.

The mental state of these cases, especially in association with their attacks, is compatible with our theory that there is a diminution of normal cortical inhibition which allows of the occurrence of the attacks, and that the crises are comparable with other phenomena of a "release" nature.

Clinical Manifestations.

Type of Case in which found.

In a previous paper [4] we made a classification of the mental types of chronic epidemic encephalitis into bradyphrenic, depressed, paranoid and behaviouristic, with certain subgroups. The usually accepted classification from a neurological approach is into extrapyramidal or Parkinsonian, pyramidal and intermediate types [15]. We can state

that oculogyric crises may appear in any of the various mental types, and further, that they show no special predilection for any of them. From the neurological side all our cases have been associated with Parkinsonism and have been fairly equally distributed amongst all degrees of this syndrome. One might have expected to find oculogyric crises more common amongst patients who showed other ocular abnormalities, a bare enumeration of which would merely be a list of practically all the signs and symptoms possible from lesions of the ocular nervous apparatus. As a matter of fact, experience does not bear out this expectation, and some of our cases with oculogyric crises are singularly free from other elements of the encephalitic ocular syndrome. This fact may be correlated with the pathogenesis of these crises, which tends to show that they are due to lesions affecting the cortical inhibitory paths and those to the ocular supranuclear centres, which means that the causal lesions may well be quite distant from the central ocular nervous apparatus itself.

It is, of course, impossible to be dogmatic on 23 cases, but certainly our experience tends to show that age and sex are quite unimportant. Fourteen of our cases are males with ages ranging from 15 to 42, while the nine females also vary from 15 to 42 years. The majority are certainly males and under 25, but this is roughly proportionate to our total cases who number 136, of whom 87 are males, and of these 63 are under 25. We consider the high proportion of our cases exhibiting these crises to be due to two causes; the first, and in our opinion much the less important, is that owing to continuous observation in a hospital the attacks are not likely to be missed when they do occur. That they are overlooked in many cases is certain, for quite a few of our patients suffered with them for long periods prior to admission, without any attention having been paid to them. The second and more important cause is that the crises are in part dependent on an interference with cortical inhibitions, the lack of which is also the cause of many of the psychotic symptoms which lead to certification.

Associated phenomena.—Oculogyric crises may occur as isolated phenomena, or may be part of a more widespread tonic seizure. In only three of our cases is the latter condition marked, and in these the accompanying spasms are confined to the head and neck. In one (Case 1) the head is turned with the eyes to the left and is somewhat retracted (see figs. 1 and 2); in another (Case 2) the head is curved backwards, while in a third the rigidity is particularly noticeable when the deviation of the eyes and head is in a downward direction. Other

observers are struck by the relatively common coincidence of associated tonic phenomena. Thus, Wimmer [16] and Marinesco and Radovici [5] found associated tonic spasms in a large percentage of their

FIG. 1.—Case 1. Oculogyric crisis showing deviation of head and eyes upwards and to the left.

FIG. 2.—Case 1. Oculogyric crisis, showing deviation of eyes up and to the left with slight turning of head to left.

cases. In all such cases it is apparent that the stimulus first attacks one of the centres of conjugate deviation and, if strong enough, overflows into associated centres to cause co-ordinated movements normally

associated with the deviation, the head always turning in the same direction as the eyes and, when torsion of the trunk and limbs have been recorded, this also has been in the direction in which the eyes are fixed. In the majority of cases a feeling of helplessness is experienced, and this is sometimes accompanied by a feeling of inability to speak, but in no case is either of these symptoms absolute. Inability to close the eyes is fairly common. The crises are accompanied almost invariably by feelings of mental discomfort, often amounting to definite distress, but physical pain is unusual. Slight headache or more commonly aching of the eyeballs, is complained of, but is of obviously minor importance to the patients. The feeling of distress appears to be a phenomenon akin to the sensation of impending dissolution experienced in angina pectoris, and in a lesser degree in some vaso-vagal attacks, one patient actually volunteering that she feels she is going to die during the crises. Another interprets it as a fear that her eyes will remain up for ever, while a patient recently admitted describes feeling as if his eyes were going right up and that he was going blind. These ideas recur during every crisis, and are doubtless similar to what Stern [11] describes as compulsive thoughts associated with tonic eye spasms. In several of our cases the crisis is accompanied by screaming or crying; in one stamping of the feet and general excitement is a usual concomitant, whilst another provides an exhibition of violence and obscene language of unusual degree, which lasts for hours after the oculogyric crisis has terminated.

These exhibitions of abnormal behaviour are such as are usually regarded as due to release from cortical inhibition, a phenomenon which we consider of great importance in these crises. Fatigue and emotion are common antecedents of individual attacks, and both are well recognized as paralysers of voluntary control, even in the healthy subject, so that it is not surprising that they are potent factors in our patients. There is abundant clinical evidence to support the thesis that lack of cortical inhibition is an important mechanism in the mental symptoms seen in encephalitics. It explains the characteristic temperament, with its childish exhibitions of temper and impulsive unthinking acts, apachism being the example *par excellence* of uninhibited behaviour. All our patients, therefore, show evidence of a general disturbance of cortical inhibition, and the majority show it in a special manner in association with their crises. This is clearly seen in certain cases where the peculiarly close association between the ocular and emotional disturbances points to some common factor bringing them more or less

simultaneously into play. We refer to the cases where maniacal outbursts immediately precede or occur at the same time as the crises, and may last for longer or shorter periods than them. In some of these patients one or other of these phenomena may occasionally occur alone, showing that they are not altogether parts of one and the same condition, and when this does occur the patient will sometimes volunteer the statement that he was surprised that either the crisis or the mental outburst had occurred alone. This association is particularly striking in five of our cases, who are simple well-behaved bradyphrenics, apart from the outbursts associated with their crises. Several of our patients were certified solely on account of periodic outbursts of uncontrollable screaming occurring at frequent intervals. In some the ocular disturbances were overlooked owing to the overshadowing mental accompaniments, and it may be that the apparently causeless outbursts of excitement and grief not uncommonly seen in encephalitics, are more often accompanied by ocular crises than is generally suspected. The importance of recognizing the association lies in the fact that whereas ordinary apachism is unaffected by hyoscine, these outbursts accompanying oculogyric crises are usually well controlled by this drug.

Position of eyes during attack.—A typical crisis occurs rather suddenly, and the eyes may become fixed in any position. Most commonly they are turned either straight up, or upwards and to either side, the downward position being much rarer (see figs. 3 and 4). Frequently the deviation is such that scarcely anything but sclerotic is visible. One case occasionally shows fixation of her eyes in a position of extreme convergence. Sometimes there may be little or no deviation, so that the attacks manifest themselves by a fixed stare to the front or slightly to one side. These attacks easily pass unobserved, and are probably commoner than is generally supposed. That these "staring" phenomena are of an allied nature to the others there is no doubt, the accompaniments being similar and the phenomena interchangeable, not only in the same patient but even during the same attack. This we consider important in locating the site of the lesion.

Of our patients eight complain of diplopia during their attacks, and one invariably asks if she looks cross-eyed. In several of our cases the eyes are carried horizontally to one side, and in two the movement is occasionally downwards and to the left. One of these is considerably more distressed by this downward deviation than by his ordinary crises, and likes his head, which on these occasions is flexed on his chest, to be pushed up. This usually results in a deviation of his eyes into the

FIG. 3.—Case 1. Oculogyric crisis, showing movement of head and eyes downwards and to the left. (The eyelids are lifted in order to show position of eyeballs.)

FIG. 4.—Case 1. General attitude in downward crisis.

more usual position of up and to the left, a position which he prefers. There is considerable rigidity of the neck muscles and resistance against extension, but when once the eyes have adopted the upward direction the head also becomes fixed in that position. This case is very definitely against Fischer's contention that the peculiar position of the neck is a deliberate posture taken up by the patient to avoid painful cramp in the eye muscles. In many of the cases the direction of the crises is not invariable. Thus, in two patients the direction is usually up and to the left, but may be down and to the left; in Case 2 the eyes may move straight up, up and to the right, or up and to the left; in another patient they generally deviate straight up, but sometimes up and to the right; in another the movement may be straight up, up and to either side, or staring attacks may occur; whilst in one patient deviation up and to the left is commonest, but the eyes may assume any direction except below the horizontal plane. On the other hand, in three cases the position is always up and to the left, while in two it is always straight up. In one patient the attacks start by a deviation to the right, which soon gives place to a purely vertical position.

Duration of attack.—The eyes may remain fixed from a few seconds up to several hours. Case 2 has been observed in a crisis lasting a whole day with only very short intermissions, and in Case 1 an attack has frequently lasted from a few minutes after waking to 6 p.m. In nearly all cases, however, the patient is able by a strong voluntary effort to bring back his eyes momentarily to a normal position and to follow a moving object to some extent.

Time of onset of attacks.—It is notable that a fairly large proportion of attacks occur in the afternoon or evening, a fact which tends to support the well-recognized view that fatigue is an important factor in their appearance. Psychical factors are equally important, and the crises are sometimes definitely reactive to psychic stimuli. In this respect they appear to occupy a mid-place between epileptic attacks which are but infrequently reactive, and such phenomena as narcolepsy and cataplexy, in which an emotional stimulus is a usual precedent. The majority of patients show to some degree a specific predilection for certain times of the day. Two cases often have them between 5 and 6 p.m., another just before going to bed at 8.30 p.m., Case 2 between 6 and 8 p.m., while Case 1, when kept off hyoscine for a week, had continuous crises from a few minutes after waking until about 6 p.m. For the rest of the evening he was quite free from attacks. Crises are not infrequently noticed at meal times, and the reason for this may be

threefold: (i) that meals in an institution are one of the excitements of the day; (ii) that this is an opportunity for the patients to show off their accomplishments and incidentally, perhaps, to be fed by a nurse owing to their consequent inability to feed themselves; (iii) that slight attacks are less likely to pass unnoticed at this time. Several patients have regular crises just before their hyoscine injections, which may be due to a combination of two factors: (*a*) the wearing off of the effects of the previous injection, and (*b*), the excitement produced by the expectation of another injection.

Precipitating cause of individual attacks.—In the majority of crises noted by us there has been no obvious precipitating cause. Exceptions to this are not uncommon, and the following incidents have been active in bringing on attacks at various times: Interrogation and expression of interest in them, or the suggestion furnished by the sight of others in attacks; excitement, temper or grief, denoting an emotional factor; general fatigue following hard work, eye fatigue following the fixation of a near object, for some time, pointing to physical or proprioceptive stimuli; and lastly, revolving during a waltz, indicating a vestibular mechanism.

Precipitating cause of initial crises.—This subject is dealt with under pathogenesis, and here we would only state that in our opinion psychogenic factors are of very minor importance in originating the phenomena under discussion, which must be regarded as due to definite lesions of the ocular nervous apparatus. In only four of our series was a history of the circumstances of the first attack forthcoming, and in none were we satisfied that a psychogenic origin could be definitely established.

Ability to abort and prevent attacks.—Apart from the ability to stop the attack momentarily by a strong voluntary effort, most of the patients are able to influence it by other means. Closure of the eyes, whether performed actively or passively, effects a temporary remission of the crisis, but on opening the eyes again the deviation and fixation may immediately re-occur. Occasionally closure of the eyes is successful in cutting short an attack altogether, especially in less severe cases; on the other hand, many of the patients are quite unable to keep the eyes closed during an attack, and some of these continue blinking violently in an endeavour to overcome the spasm. In Case 2 this blinking has recently become so persistent that the fixation of the eyes is completely overshadowed, and she wanders about the ward with an anxious expression, blinking rapidly in what is often a vain

attempt to prevent her eyes going up. Some patients lie down and cover their heads with a rug or blanket in order to facilitate closing of the eyes. The recumbent posture has been said to relieve or even cut short the attacks in some patients, but we have only met with one case in whom lying down alone, without closure of the eyes, had any beneficial effect. Apart from these methods of influencing the attacks, which are common to nearly all the cases, many individual experiments have been tried with varying results. There is no doubt that suggestive means are at times successful in cutting short attacks; in our series, injections of water, inhalation of amyl nitrite, threats of not being allowed week-end leave, or of being stopped going to a dance, and in one case the threat of having cold water thrown over him, have all at times brought about the cessation of an attack. In others such methods have been singularly unsuccessful. Thus, one patient, who had frequent slight attacks from the time of admission, was soon sent to the ward in which the majority of the encephalitics were. Here he could see for himself the benefit of injections, and soon began to beg that he might have them. He was encouraged to believe that an injection would put a stop to his crises, and after some days an injection of water was given. To his genuine surprise and disappointment it had no effect. Later hyoscine $\frac{1}{100}$ gr. was given orally, and this effected the inhibition of attacks for thirty hours, and also brought about considerable improvement in his speech and general activity. Two or three days later a dose of aqua chloroformi made up to taste like the hyoscine mixture was given, and though the patient was told that this was exactly the same medicine as his previous dose, he stoutly maintained that it was no good. Belladonna was then tried over a period of a week, but, compared with hyoscine, the effect was very slight. Further experiments have confirmed these results, and it is clear that in his case hyoscine alone influences his attacks to any extent. Despite this example, we agree with Marinesco and Radovici [5] that it is especially those patients who have had no experience of hyoscine and kindred drugs who respond best to therapeutic suggestion. As soon as they have learnt at first hand the effects of such drugs, they are influenced by no others. Several of our patients whose attacks could at first be controlled to some degree by suggestion of various kinds, are no longer in the least susceptible to these methods. Besides the actual cutting short of attacks, psychical factors have a considerable influence in their complete prevention. Thus, one patient whose crises occur several times a week in the afternoon, has never been known to have one on

dance days, whilst another exhibits the same freedom from attacks on days when there is physical drill. Isolated incidents such as these would be quite wrongly interpreted if they were taken to point to malingering. The intensity of the attack appears to have little relation to the effect of psychical factors, and we have at times been able to cut short the severest crises by therapeutic suggestion, whereas at others quite mild attacks in the same patient were completely uninfluenced by such means.

Pathogenesis.

Physiological anatomy of conjugate movement.—It is not proposed to attempt a full description of the physiological anatomy of conjugate deviation. The literature on this subject is extensive, and as no two authorities agree as regards details, only a short summary of the more important views will be given.

Higher centres for conjugate deviation.—Conjugate deviation not only responds to volition, but can also be a reflex response to vestibular, visual, auditory, tactile and proprioceptive stimuli. Starting from above downwards, there is a definite area in the second frontal gyrus which appears to be concerned only with voluntary movements, whilst other cortical centres for conjugate deviation have been described by Ferrier in the angular gyrus, and by Schäfer in the visual area of the occipital lobe. Knoll and Topolanski found that electrical stimulation applied behind the posterior commissure produced conjugate deviation of the head and eyes to the stimulated side, and later Graham Brown showed that stimulation of the mid-brain in front of the posterior commissure brought about a deviation to the opposite side. Muskens [6] considers that the fibres subserving this lateral conjugate deviation are pallido-fugal, passing by Forel's bundle to posterior commissural supravestibular nuclei, and he considers it the main tract for lateral locomotion and lateral deviation of the eyes. He and others [14] hold that the fastigial nucleus (nucleus tecti of cerebellum) is a primary vestibular centre concerned in the movements of falling backward and looking upward, and that the centre for falling forward movements is near the raphe of the medulla oblongata [7]. He considers that the frequent combination of tonic lateral positions of the eyes with the upward and downward position points to the lesion being where the fibres involved in these two forms of forced movement come close together, viz., just in front of the posterior commissure near the median line, i.e., in the metathalamic region.

Oculomotor nuclei.—The oculomotor nuclei lie in the grey matter of the floor of the aqueduct of Sylvius. Le Gros Clark [3], from a study of their comparative morphology, is of the opinion that the functional elements of the oculomotor nuclei are more probably arranged dorso-ventrally than antero-posteriorly or from above downwards, and suggests that much of the confusion amongst different workers is due to a non-recognition of this fact. He further infers that there is a localization of movement rather than of individual muscles in these nuclei, inward movement or convergence by the internal recti being represented in the paramedian group of cells (nucleus of Perlia) [9], dorsal or upward movement in the dorsal group, and ventral or downward movement in the ventral group. This certainly harmonizes the otherwise divergent views of many observers and agrees with his findings in the field of comparative anatomy. It should be noted, however, that some observers [8] actually reverse these localizations.

Associational and reflex apparatus.—More important in the present context than this probable anatomical localization of cells subserving conjugate movements must be the association fibres which distribute the impulses necessary for these movements. Amongst the most important of these is the dorsal longitudinal bundle which connects the motor nuclei of the ocular nerves with Deiters' nucleus (vestibular); the ascending ventral columns of the spinal cord (proprioceptive); fibres from cells in the tegmentum and the anterior corpora quadrigemina (visual reflexes) which can be traced anteriorly into the subthalamic region and, according to Fraser, into the thalamus itself. Conjugate lateral movements of the eyes are regarded by most authorities as being subserved by a mechanism distinct from that of vertical movement, and this might be expected from the very different combination of muscles used in the two phenomena. The most generally accepted view is that fibres arise in the abducens nucleus and ascend in the dorsal longitudinal bundle of the same or of the opposite side to reach the oculomotor nucleus, and pass out with the third nerve to the opposite internal rectus, thus explaining the invariable working together of the external rectus of one eye and the internal rectus of the other eye [2]. Another hypothesis, which fits the known facts better and is supported by Gordon Holmes, postulates a supranuclear centre in the region of the abducent nucleus which receives impulses from all sources which can cause conjugate deviation of the eyes to the same side. To this centre come voluntary impulses from the opposite frontal centre, visual and auditory reflexes from the corpora quadrigemina, vestibular reflexes

through Deiters' nucleus, and proprioceptive stimuli from the muscles of the head and neck. In this supranuclear centre these impulses are correlated and co-ordinated, and pass on by efferent fibres for the stimulation of the motor nuclei of the corresponding internal and external recti muscles and for the reciprocal inhibition of their antagonists. Clinical evidence in favour of this hypothesis is seen in cases on record, where these various fibres of different function have been injured separately with, in some patients, abolition of the reflex of turning the eyes following labyrinthine impressions, while power of voluntary deviation remained intact, and in others a reversal of this phenomenon. In the same way can be postulated a supranuclear mechanism for upward and downward movements of the eyes. One hypothesis is that this is situated in the anterior corpora quadrigemina, another that it is in the tegmentum or in the central grey matter around the aqueduct of Sylvius.

General considerations.—In the isolated cases reported in the literature no attempt has been made, as a rule, to discuss the pathogenesis of these attacks. In the somewhat analogous respiratory anomalies the suggestion was frequently made that these were merely hysterical manifestations. No one, so far, seems to have put forward this untenable hypothesis in connection with the oculogyric crises, but as several continental writers [13] [16] favour the view that they are what they call "hysteriform" in character, it would be as well to say a few words on this theory. They do not deny an organic substratum, but consider that the resultant phenomena are produced by the same mental and physical mechanisms as are the grosser physical manifestations of hysteria, such as anæsthesia, paralyses, tics, &c. They maintain that the original onset of the crises in each patient is probably always due to a superadded factor of psychic importance, e.g., a strong emotion, physical or intellectual fatigue, or, and this they consider very important, mental contagion from witnessing a crisis in a fellow patient. In our series of cases this has been the exception, the majority of the patients finding it very difficult or impossible to say when they first experienced a crisis. These authors stress the effect of suggestion in precipitating attacks, and of therapeutic persuasion in cutting them short. Here, again, our experiences do not agree, as we find suggestion quite powerless to initiate an attack in the majority of our patients, and therapeutic persuasion a very variable weapon in cutting them short. There is manifestly a considerable psychical disturbance associated with many of the attacks, just as epileptic fits, attacks of migraine, sea-

sickness, &c., are accompanied and often preceded by similar emotions. It appears to us more reasonable to class these disturbances as part of the attack than as the responsible agents, although it is admitted that emotion, fatigue and excitement may have at times a precipitating effect. This is only to be expected if the hypothesis about to be put forward be a correct one. Unlike our patients, the cases met with by these authors would appear to have contraction of the neck muscles in practically every case, and very frequently the trunk and limbs are also involved, bizarre attitudes being common during the crises. In one case described the oculogyric crises alternated with attacks of hysterical spastic paraplegia lasting for a quarter to half an hour, attacks which the authors say could often be terminated by simple suggestion or injections of distilled water [16]. One would imagine that it must be extremely difficult in such a case to say that the cessation of so short an attack was due to the treatment. It must be granted that there is undoubtedly a similarity between the results of precipitating and inhibitory factors in encephalitis and pithiatism. This has already been pointed out by Turner and Critchley [12] in their study of encephalitic respiratory disorders, and with them we would emphasize that this similarity should not be strained. If these phenomena in our patients are to be regarded as somewhat similar to hysterical manifestations, it should be in the sense that oculogyric crises and analogous encephalitic phenomena point very strongly to hysteria having a physical basis and not being the purely psychical disease it is usually considered. It is not necessary to postulate gross histological changes in and around the basal ganglia in hysteria, but subtle biophysical or biochemical changes in this region may well be present. Variability of symptoms depending on suggestion and emotional factors is by no means confined to hysteria, but is present in practically all organic diseases of the nervous system in greater or less degree. It does not, therefore, seem necessary to postulate or emphasize a psychical origin for these phenomena when they appear in encephalitics any more than when they are found in other organic nervous disorders.

Can we find any organic explanation for the increased suggestibility of the encephalitic? Whilst our cortical centres and their centrifugal paths are intact, we react to external stimuli after an intellectual elaboration by an adequate voluntary movement or by a motor inhibition, in either case arriving at a definitely pursued end. When a functional or organic alteration upsets the normal harmony, the reaction of the individual to the same stimuli reveals a pathological condition. There

is no doubt that the diffuse lesions of the extra-pyramidal system and of the higher vegetative centres set up a new state of function. Lesions of the basal ganglia and neighbouring grey matter must be held responsible for the Parkinsonian rigidity, the slowing and abolition of automatic movements, and the abolition of mimicry and of emotional expression. And in the same way there is little doubt that the lesions of these same centres and of their connections with the cerebral cortex also cause interference with cortical control with resultant psychical disturbances in these patients. Here Pavlov's researches on the conditional reflex have some bearing. He found that lesions of the cortex cause a much greater interference with the inhibitory than with the excitatory impulses, an important fact when it is remembered that many encephalitics have diffuse cortical lesions in addition to the more usual lesions elsewhere. The inhibitory cortical fibres in the encephalitic being thus partially destroyed, external stimuli reaching the subcortical centres are more easily translated into the movements subserved by this part of the brain. The lesions of these basal centres can, therefore, be regarded as the anatomical basis of the psychic phenomena and especially of the increased suggestibility of these patients. The various tonic crises which appear spontaneously in our patients, whether they be striatal fits, ocular spasms or respiratory crises, seem to us to be an expression of this same abnormal functioning of certain subcortical centres, and the varying types of crises found are due to different parts of the area being affected. Two of our encephalitic patients have had fits of extra-pyramidal type, and in spite of Collier's [1] arguments against this type of epilepsy, we agree with Spiller [10], Sterling, and those others who are of opinion that it is due to lesions in the subcortical centres. This same mechanism of liberated function explains equally well the myoclonias due to liberation of the bulbo-medullary motor centres, and the respiratory anomalies due to liberation of the respiratory centres. The occasional appearance of these crises following mental contagion finds a ready explanation in this same cortico-nuclear disintegration with the interruption of the cortical inhibitory fibres. In the same way abnormal suggestibility due to the interruption of the cortico-thalamic inhibitory fibres tends to emotional facility, sometimes seen in an exaggerated form as spasmodic laughing and crying. We can also conceive that a similar partial independence of the motor centres related to standing, walking and other such phenomena, is at the base of the strange paradoxical reactions found in some encephalitics. It is probable that this same mechanism of cortico-

nuclear disintegration governs all phenomena of suggestion, and that in hysteria the afore-mentioned biophysical and biochemical disturbances favour the appearance of this exaggerated subcortical functioning. Suggestibility is the expression of a dynamic state impossible to define with particularity in the present state of our knowledge, but one feels that the study of the encephalitic is likely to prove one of the most fruitful fields in the elucidation of this problem.

Distinct from the lesions causal of this increased suggestibility, we must also postulate lesions which determine the type of subcortical fit taking the form of oculogyric crises. If there are separate supranuclear mechanisms for lateral and for vertical conjugate movements, then the lesion causal of oculogyric crises probably does not lie in any of the supranuclear centres, but in some higher associated mechanism. We are led to presume this from the fact that not only may the eyes take up any position in different attacks, but that even in one and the same attack they may change from the lateral to the vertical position or vice versa, or in some cases to staring straight ahead. In one of our cases (Case 2) the position of the eyes on rare occasions was one of convergence. Such varying positions would scarcely be found if the lesion were limited to one or other supranuclear centre subserving certain movements only of the eye ; and it is unlikely that in these cases there are various lesions in the different supranuclear centres. The inhibitory influences normally coming from the cortex being, as we have seen, interfered with, the other impulses which act on the conjugate mechanism find it easily influenced. Here we would state that we cannot agree with Muskens in neglecting the proprioceptive, auditory, visual and vegetative reflexes which act on the supranuclear centres and in regarding the vestibular apparatus as the only one involved. This he does by identifying the crises with the forced movements and forced positions seen in the lower quadrupeds after lesions of the supra-vestibular structures. He lays emphasis on the fact that the French school of neurologists have reported cases, illustrating all varieties of forced movements and forced positions, which from animal experiments have been postulated as being likely to occur with partial lesions of the supra-vestibular centres near the posterior commissure and of their palæostriatal connections. As already stated, our clinical findings do not agree concerning the prevalence of these associated movements. Even if they are only secondary or associated phenomena, their occurrence does not show that the original disturbance causing the ocular spasms is in the vestibular system. Also it is always dangerous

to draw conclusions from experimental work in animals which is still far from being proved. His contention that the lesion is in the metathalamus cannot therefore be accepted as final, and more work is necessary before the causal lesion can be assigned to any definite area or areas. Here it may be mentioned that Levy, Hunt, Vogt, Stern and von Economo think that forced positions in the vertical plane point to lesions in the corpus striatum, and that Tritiakoff, Marinesco, Goldstein, Claude, Holman, MacKinlay and Gowan, on various grounds, place the lesion causal of the crises in the body of Luys.

In suggesting the above hypothesis we do not wish to appear dogmatic. Theorizing is always tempting, but as we do not propose to bring forward evidence in support of any other views, we will merely mention two which appear to us to possess attractive possibilities. Thus, we consider it quite feasible that the metabolic dyscrasia known to be present in chronic encephalitis leads to the setting free of substances which act on the nervous system in the same manner as convulsant poisons. Or, again, we may be dealing with a local vasomotor spasm, and in support of this there is the well-recognized disturbance of the autonomic system in the encephalitic, as seen in the vagotonia of Parkinsonism.

Prognosis.

No definite prognosis as to how long the crises are likely to persist can be given in any individual case, but in a considerable proportion the crises tend to disappear, or become very much less frequent and severe, after treatment by hyoscine. In our series of twenty-three cases, sixteen have attained complete freedom from, or very marked diminution in the frequency and severity of, their crises. This improvement is maintained in six of these patients, even when hyoscine is withdrawn; in five the crises return on omitting hyoscine, and in the remaining five withdrawal of hyoscine has not yet been tried. In five who have been on hyoscine for a considerable time the crises, which are in each case infrequent and mild, have appeared since the administration of this drug was begun. These crises are apparently uninfluenced by hyoscine or any other form of medicinal treatment, but it is of course possible that their attacks might have been more severe were it not for the influence of the drug. One case who had mild staring attacks before the administration of hyoscine still remains unaffected, while the remaining case has been admitted too recently to be classified here. Thus it will be seen that only one out of eighteen patients whose

attacks developed before hyoscine treatment was given remains uninfluenced, compared with sixteen who show undoubted benefit. It is noteworthy that the six cases which at one time were very severe have all progressed very favourably, and that two of them are very much improved, even when hyoscine is withdrawn. The mild infrequent types are relatively the more intractable. The improvement or otherwise as regards these crises shows no correlation to the other symptoms of the disease, and seems to be quite independent of the general progress of the encephalitic process. It may be that the improvement has been effected by a natural process—perhaps an irritative lesion in the brain has become inactive, and that even without hyoscine the spasms would have disappeared. In this respect it is interesting to note that Turner and Critchley [12] found that nearly 50 per cent. of encephalitic respiratory anomalies showed spontaneous cure after a few years. On the other hand, it is possible that the hyoscine, by preventing the attacks over a considerable period, ultimately breaks the reflex "habit," so that later it can be withdrawn with impunity, an action similar to that which appears to be operative in some cases of epilepsy treated with bromides or other sedative drugs.

The second question in prognosis which arises is as to what significance, if any, the onset of oculogyric crises has on the disease as a whole. Should such crises be regarded as making the general outlook for the patient more serious, or should they be regarded more as an intercurrent complication having little or no general prognostic significance? From our experience we incline to the former view. We have found nothing to suggest that these attacks portend a more rapid progress of the chronic encephalitic process, though their onset does afford a reminder that we are dealing with an actively progressive condition. But we would suggest that the real significance of these crises is to be found in the relatively high proportion of these patients who ultimately require certification. Though histological proof is so far lacking, we are probably safe in assuming that when the encephalitic process spreads to the higher centres of the brain, psychotic symptoms become a definite possibility. The proportion of certified encephalitics who have oculogyric crises is certainly higher than amongst non-certified cases, and this we think may be due to the fact that the crises and many of the psychoses result from lesions causing loss of cortical inhibition. The onset of these attacks points to an active spread of the encephalitis, and the possibility of psychotic symptoms must then be borne in mind in giving any prognosis.

Therapeutics.

As in Parkinsonism, the atropine group is unrivalled in its effect, and the majority of cases can be kept free from crises over long periods by judicious use of these drugs. The greatest measure of success is obtained by subcutaneous injections of hyoscine. After very extended trial under careful observation, we have come to the following definite conclusions regarding the use of drugs in Parkinsonism. Belladonna and stramonium can be discarded, as in the few cases where they give any appreciable benefit better results can be obtained from hyoscine by the mouth, or genoscopolamine. Of these two the latter is more generally useful and should always be tried before resorting to injections of hyoscine. With very few exceptions, cases which benefit by these oral methods benefit still more from hyoscine given hypodermically, but for obvious reasons this should only be resorted to if the improved results are great enough to warrant it. In the advanced cases it will be generally found that the injections are infinitely superior and therefore justified. It is important that the smallest efficient dose should be discovered by experiment in each case, and we have even found $\frac{1}{1000}$ gr. hyoscine hydrobromide by the mouth every other day sufficient in some cases. The majority of our advanced Parkinsonians require $\frac{1}{100}$ gr.— $\frac{1}{75}$ gr. hypodermically twice or thrice daily. The greater efficacy of injections in oculogyric crises is even more noticeable, and here genoscopolamine has proved rather less successful than hyoscine by the mouth. Therapeutic suggestion is generally to be avoided. Though sometimes successful at first, it is unlikely that the patient will respond to this form of treatment for long, as encephalitics are notoriously alert concerning their treatment and are very quick in finding out if they are being tricked. They are then hurt at the way they have been treated, and are inclined to lose faith in the physician and any treatment he orders. For this reason our experiments with therapeutic suggestion have been as few as possible.

Summary.

(1) Oculogyric crises are unknown apart from epidemic encephalitis, and it is only of comparatively recent years that they have occurred. In our series the earliest case commenced in 1923, and the earliest epidemic which led to a case was that of 1919. The shortest interval between the acute attack and the appearance of the crises has been a few months, and the longest eight years.

(2) These crises are not associated with any particular mental type of encephalitis, but so far they have not been described in a non-Parkinsonian case. Other ocular symptoms are not more frequent than in the ordinary encephalitic without crises.

(3) The crises are in the nature of tonic seizures and need not be confined to the eye muscles, a more or less co-ordinated spread to the muscles of the head and neck being not uncommon. Physical pain is an unusual concomitant, but psychical distress of various kinds is very common.

(4) The eyes may become fixed in any position, and this position may change during a crisis, or from one crisis to another. In one case the eyes took up a position of forced convergence, and in three a fixed stare to the front has been observed. This variability is important in determining the site of the lesion.

(5) The duration of the attack varies from a few seconds up to several hours, and attacks in the same patient may vary considerably in this respect.

(6) The majority of patients show a predilection for certain times of the day, and this is doubtless to be correlated with the effect of fatigue and emotion as determinants of attacks. In the majority of attacks no precipitating cause can be found.

(7) It is occasionally possible to shorten or prevent attacks, and suggestion is the most potent agent in this respect. Each patient usually finds some means of allaying the discomfort incident to the crisis, lying down with eyes covered being the most common.

(8) It is misleading to regard these crises as hysteriform in nature. The undoubted similarity between the results of precipitating and inhibitory factors in hysteria and encephalitis should not be strained, as variability of symptoms depending on suggestion and emotional factors is not confined to hysteria, but is present to some extent in practically all diseases of the nervous system.

(9) The increased suggestibility of the encephalitic is due to an interference with normal cortical control and a cutting off of its inhibitory influence.

(10) The abolition of cortical inhibition explains the release phenomena of different subcortical centres manifested clinically as tonic fits, ocular spasms, respiratory crises, myoclonias, emotional facility, paradoxical reactions, &c., the particular manifestation depending on the site of the lesion.

(11) The causal lesion of oculogyric crises lies in associational

mechanisms situated above the four supranuclear centres subserving conjugate movements, the theory being accepted that there is a supranuclear centre for lateral conjugate movements, and one for vertical movements on each side.

(12) The effect of emotion on the crises is probably indirect, brought about by an inhibition of the already enfeebled inhibitory fibres from the cortex.

(13) In a certain proportion of the cases the crises tend to disappear with time, and this is especially so in cases treated with hyoscine.

(14) A large proportion of encephalitics who suffer from oculogyric crises subsequently require certification, a fact which should be correlated with the loss of cortical inhibition in these crises and in encephalitic psychoses.

(15) Hyoscine administered hypodermically is the most generally useful method of treatment in this, as in other Parkinsonian phenomena, but it should only be used under careful supervision and in selected cases.

Representative Cases.

Case 1.—J. W. B., male, aged 15, was admitted to West Park Mental Hospital, August 16, 1927. His encephalitis appears to date from 1923, and in 1926 deficient cortical inhibition became prominent in a liability to fits of uncontrollable temper, impulsive violence and frequent threats of suicide. This led to his certification in 1927, when he was admitted to Warwick County Mental Hospital. During his three months' stay there he is reputed to have been dull, listless, vacant and of very slow cerebration. Parkinsonism appears to have advanced quickly in 1926, and on admission here was so marked as to render him quite helpless and unable to stand unaided. There was a left-sided hemiplegia, including the left side of face. Cogwheel rigidity was well marked. The head was held flexed on the chest and turned to the left. No tremor was observed. Voice was slow, monotonous and very indistinct; salivation was excessive.

Ocular system.—The pupils are equal, regular and react normally to light and on accommodation. No deficiency of convergence is present. Eye movements are fairly smooth, but there is some difficulty in looking to the extreme right. Upward movement is good, but there is a total inability to wrinkle the brow. Some blepharospasm is present on closing eyes. There is no strabismus, nystagmus or ptosis. Diplopia is complained of during oculogyric crises. The fields of vision and fundi are normal. On admission his apache tendencies were not in evidence, and his most prominent mental symptoms were bradyphrenia tinged with a mild degree of reactive depression. An immediate mental and physical improvement was effected by injections of hyoscine, $\frac{1}{150}$ gr. once a day, and he was very shortly able to get about, feed and dress himself, and generally take an interest in life. He is now very active and can

walk and run well, although with a limp. Rigidity of neck muscles and carriage of head was rather intractable at first, but has now been much improved by massage and electricity. On the withdrawal of hyoscine, even if for a single day, he reverts to a condition of helplessness and misery similar to his state on admission.

Oculogyric crises.—These first started about a fortnight before he left Warwick County Mental Hospital, in May, 1927. The patient noticed that he was occasionally unable to follow the lines of a book he was reading, but if he got up and walked about for a while his eyes would recover. On admission to West Park crises were very severe, frequent and of many hours' duration. A complete inhibition was rapidly effected by means of injections of hyoscine. On withdrawing the drug for a week, regular and severe attacks recommenced and lasted from a few minutes after waking until about 6 p.m. The deviation was sometimes upwards and to the left, and at others downwards and to the left. The head was turned towards the left and held rigidly in a position of flexion or extension, depending upon the position of the eyes. The omission of hyoscine even for one day invariably results in the appearance of ocular crises. There is no local pain or discomfort, but considerable mental distress is evident. Diplopia is sometimes complained of during attacks, and shutting the eyes is impossible. Lying down, covering the eyes or blinking have no effect upon the spasms. Soon after admission an attack was cut short by the inhalation of amyl nitrite, but this has never succeeded since that occasion Several other forms of therapeutic suggestion, including injections of water, have been tried and the results have been invariably unsuccessful. Vestibular tests were carried out actually during a crisis. Both in the rotatory and the caloric tests giddiness and vomiting were very easily produced. It was found that no nystagmus could be evoked away from the side to which the eyes deviated (i.e., the left), that is to say, after rotating the patient to the right nystagmus to the left was observed, but after rotation to the left there was no nystagmus. The caloric tests similarly failed to produce nystagmus to the right. Between the crises the vestibular reactions were normal.

Case 2.—E. B., a girl, aged 14, was admitted to West Park Mental Hospital, on December 3, 1927. She had her acute attack in April, 1924, and Parkinsonism appeared in the following year. Her condition progressed and she became increasingly psychotic and difficult to manage, with symptoms pointing to "release" from cortical inhibition. Suicidal tendencies developed and she was admitted to West Park. She showed a fairly advanced state of Parkinsonism (R > L), with coarse tremor, monotonous speech and excessive salivation. She was on the whole bright and cheerful, except around the period of her oculogyric crises.

Ocular system.—The right pupil is larger than the left. Reaction to light is good and accommodation reflex and power of convergence only slightly defective. Eye movements are jerky and ability to look upwards is impaired. She is quite unable to wrinkle her brow. A few nystagmoid jerkings are noticed on looking to the extreme sides. Some blepharospasm is occasionally seen but

there is no ptosis, strabismus or diplopia. Fields of vision and eye grounds are normal.

Oculogyric crises.—These were noticed early in 1927, at Winchmore Hill, but the patient states that she had her first attack about three months after her illness began. She describes how she was playing with a girl friend at putting their faces in peculiar positions, and that on copying her friend's effort she got her eyes up and could not get them down again until supper time (about four hours). On admission to West Park the attacks were severe, and at one time she remained with her eyes fixed in a tonic spasm throughout several days, with only brief and infrequent intermissions. Her sleep, however, was not interfered with, and during this the condition relaxed. For a few days not even injections of hyoscine had any influence on the attacks, but at length they stopped of their own accord. A few days later they recommenced, and since then they have been fairly well controlled by hyoscine. The attacks were associated with extreme distress and often screaming. She liked to go to bed and put her head under the clothes to assist her to close her eyes, a performance of great difficulty to her. If bed were not allowed immediately she would scream and bang her head on the floor or on the furniture in order to get her way. The deviation was straight up, or up and to either side. Of late her crises have been few and mild, but about half an hour before the injections of hyoscine she starts blinking rapidly and persistently, at the same time walking round the ward with her head hyperextended and an extremely worried expression on her face, and constantly asking the nurses whether she is looking cross-eyed. On two occasions she has been observed with her eyes fixed in a position of extreme convergence. This type of crises, which has not been seen in any other case, brings with it an exceptional distress. The patient cries bitterly and is genuinely frightened and miserable. Vestibular tests were carried out during a crises with results similar to those in Case 1.

Case 3.—H. R. D., male, aged 22, was admitted to West Park Mental Hospital, on April 12, 1928. His primary illness, four years ago, was of gradual onset, and he was able to work up till two years ago. On admission he showed a moderate degree of Parkinsonism, with characteristic speech, facies, posture, shuffling gait and sialorrhœa. Mentally he belonged to the behaviouristic group, with the typical encephalitic temperament. His conduct changes were closely associated with his oculogyric crises, and pointed very strongly to a common factor being present in both phenomena, the factor in our opinion being impairment of his power of cortical inhibition.

Ocular symptoms.—His pupils are equal, but irregular in outline; they react normally to light, but very poorly on accommodation; there is practically no power of convergence. Movements are slow and jerky with some impairment of the power of looking up. Slight blepharospasm is present, but no nystagmus, strabismus or diplopia. Double ptosis of varying degree may be seen. Wrinkling the brow is extremely defective. The visual fields and eye-grounds are normal.

Oculogyric crises.—These started two years ago and have recently occurred

three or four times a week. They are accompanied by fits of violent and uncontrollable temper, in which he uses foul language and resorts to screaming, biting and kicking. The onset of excitement usually anticipates the crisis and always outlasts it considerably. The average attack starts in the afternoon and lasts till nightfall, but during this period the eyes may only be fixed for about an hour. The deviation is usually straight up, but may be up and to either side during the same attack. During the crises there is difficulty in shutting the eyes, but no actual pain is experienced. During the first eleven days after admission he had six attacks of excitement with ocular spasms. He was then put on genoscopolamine pills, and during a period of three and a half weeks he had only three attacks of excitement, and nothing but momentary fixation of the eyes.

Case 4.—D. D., male, aged 17, was admitted to the Manor Institution on February 20, 1925. In 1919 he had an acute attack of encephalitis, followed some years later by conduct changes, irritability, moral deterioration and occasional epileptiform seizures. He was from all accounts an especially bright boy before his illness, and intelligence and other tests show that he continued his mental development for some time after the onset of his encephalitis. He is now of the apache type with the typical encephalitic temperament and evidence of a certain degree of intellectual deterioration. He is irritable, quarrelsome and lacking in control, and has been found attempting indecent exposure and abnormal acts. His Parkinsonism is confined to the upper part of his body, and is the least marked of all our cases.

Ocular system.—The pupils are irregular and unequal (R > L); they react briskly to light but sluggishly on accommodation. Convergence is only fair. The ocular movements are fairly smooth and rapid, but there is an ill-sustained rapid oscillation on looking up and a few nystagmoid jerkings on looking in other directions, especially up and to the right. The range of upward movement is defective, but wrinkling the brow is fairly well performed. No blepharospasm or ptosis is present. The visual fields and fundi are normal.

Oculogyric crises.—These first occurred as early as 1923, about the time his apache tendencies first developed. He describes how he used to have attacks when coming home after a hard day's work on a farm. On admission they used to occur about once a week, but increased in frequency until they became almost daily incidents. The position was invariably up and to the left, and the time of day always late afternoon or evening. They annoyed him and made his eyes ache, but caused no real distress. He was able to stop them temporarily by tightly screwing up his eyes. They have now been reduced to a minimum by means of genoscopolamine and are very rarely seen. At one time threats of removing certain privileges were successful in producing a strong enough voluntary effort to check an attack, but later these means became useless.

Case 5.—A. W. A., male, aged 22, was admitted to West Park Mental Hospital on February 7, 1928. He had a mild primary attack six or seven years previously. Parkinsonism and oculogyric crises were first noticed about

three years ago, while fits of excitement and temper began to occur several months later. He is of the bradyphrenic type and exhibits the characteristic childish, sympathy-craving temperament. Except for acute excitement associated with his crises, there are no definite conduct disturbances; he exhibits a mild degree of Parkinsonism and bradykinesia.

Ocular system.—The left pupil is oval, but the reactions to light and accommodation are unaffected, and convergence is normal. Movements are rather jerky and there is considerable deficiency in the upward range. Wrinkling the brow is much impaired. No nystagmus, ptosis, strabismus or diplopia are present. Blepharospasm is very much in evidence and blinking attacks occur. Fields of vision and eye grounds are normal.

Oculogyric crises.—These are said to have come on about four years ago and were noticed by the patient's father and mother three years ago. They occurred about twice a week, and were often associated with excitement and temper which usually preceded as well as accompanied the attack. The patient states that his first attack occurred while he was on the stairs at home, and he can suggest no cause for it. He covered his eyes with a mackintosh and lay down and the crisis passed off in ten minutes. During the first year or two no excitement was evident. There is no pain and only a slight feeling of discomfort. There is, however, considerable distress, the patient describing a sensation that he is going blind. Since admission he has had several fits of violent excitement and temper lasting one and a half hours, sometimes with and sometimes without fixation of the eyes. Hyoscine injections are successful in cutting short or preventing attacks.

In conclusion, we take this opportunity of thanking Dr. Norcliffe Roberts, Medical Superintendent of West Park Mental Hospital, and Dr. E. S. Litteljohn, Medical Superintendent of the Manor Institution, for allowing us to publish the cases, and Dr. F. Golla for his unfailing interest in our investigations.

REFERENCES.

[1] Collier, J. S. Lumleian Lectures, *Lancet*, April, 1928, **1**, 688.
[2] Duval and Laborde. "De l'innervation des mouvements associés du globe oculaire."
[3] Le Gros Clark, W. E. *Journ. of Anatomy*, **55**.
[4] McCowan, P. K., and Cook, L. C. *Lancet*, 1928, **1**, 1316.
[5] Marinesco, G., and Radovici, A. *Journ. de Neurol. et Psych.*, 1926, **26**, 259.
[6] Muskens, L. J. J. *Brain*, 1922, **45**, 454.
[7] *Idem. Journ. of Neur. and Psychopath.*, 1927, **8**, 136.
[8] Paton, Leslie. *Brit. Journ. of Ophthalmol.*, 1921, **5**, 253.
[9] Perlia. *Graefe's Arch. v. Ophthalmol.*, 1889, **55**, 35.
[10] Spiller, W. G. *Brain*, 1927, **50**, 171.
[11] Stern, F. *Arch. f. Psych. u. Nerv.*, 1927, **81**, 522.
[12] Turner, W. A., and Critchley, M. *Journ. of Neur. and Psychopath.*, 1928, **3**, 266.
[13] Van Bogaert, L., and Delbeke, R. *Journ. de Neur. et Psych.*, 1926, **26**, 266.
[14] Van Gehuchten, Jr. *L'Encéphale*, 1925, **20**, 530.
[15] Wimmer, A. "Chronic Epidemic Encephalitis," London, 1924.
[16] *Idem. Acta Psych. et Neur.*, 1926, **1**, 173.

OBSERVATIONS UPON THE VASCULARITY OF THE HUMAN OCCIPITAL LOBE DURING VISUAL ACTIVITY.

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For many years it has been suspected, though never adequately proved, that the rate of flow of blood through the brain increases as a result of sustained mental effort. This belief is in harmony with the increase in the metabolic exchange of human beings which appears to occur during vigorous intellectual activity [Becker and Olsen, 1914; Day, 1923; Gillespie, 1924; v. Liebermann, 1926]. Such an increase, however, may be due in part, or possibly wholly, to the increased muscular tension developed during sustained mental effort, and while precautions have been taken to exclude this factor [see especially Gillespie, 1924], observations upon the point are still equivocal [for early observations and a discussion of the literature, see Benedict and Carpenter, 1909].

Recently evidence bearing upon the vascular supply of the brain has been adduced from quite a new angle. It is well known that some portions of the grey matter of the central nervous system are much more richly supplied with capillaries than other parts. In a series of important investigations Craigie [1921, 1924, 1925, 1926, 1927] has found that the vascularity of the brain-stem and cerebellum of animals is much less at birth than after five days of life or than at maturity. Moreover, the relative vascularity of the various centres within the brain-stem does not differ much at birth, while marked differences occur in adults. A similar, though slightly less marked, increase in vascularity occurs in the cerebral cortex of rats during the first days of life. Craigie believes that the vascular richness of the various parts of the brain is related to functional activity, and that the increase which he has found in localized regions is due to increasing metabolic demands of those parts associated with activity, the nutritional requirements for functional activity being greater than for growth. In the medulla the sensory nuclei are more richly vascularized that the motor, a relation which

undoubtedly is to be accounted for by the more continuous activity of the sensory neurons as contrasted with the less frequent activity of the motor neurons.

It becomes, therefore, a problem of great interest to know whether, during the reception of sensory impulses, the centres affected become more richly supplied with blood than when resting. Also, if such an increase occur, one would like to know whether it is local or due to a generalized increase affecting the whole brain. These two problems have lately been investigated by Cobb and Talbot [1927], who have studied the magnitude of the capillary bed in the motor cortex in the visual area and in the olfactory bulbs of a series of animals which, immediately before death, were subjected to vigorous *olfactory* stimuli. The animals were injected at the time of death, and the micrometric method of Vogt applied for estimation of the relative areas of the capillary bed. In the unstimulated animals the olfactory bulbs showed 110 micra of open capillaries per 100,000 cubic micra of brain substance. Ether-stimulated animals, on the other hand, showed 149 micra, while ammonia-stimulated animals showed 171 micra. The motor cortex and the visual areas of the occipital lobe, on the other hand, showed no change under olfactory stimulation. These observations, though possibly open to the objection that an irritating stimulus was used, are significant, and suggest that vigorous sensory stimulation of a given centre in the brain is associated with an increased blood-supply to that centre.

The following case, recently under observation at the Peter Bent Brigham Hospital, Boston, Mass., appears to throw further light upon the problem of altered vascular supply of localized areas in the brain during functional activity.

Case 1.[1]—*P. B. B. H. Surg., Nos.* 26137 *and* 29731. *Headache, failure of vision with right homonymous hemianopsia; bilateral external carotid ligation; left occipital osteoplastic exploration; disclosure of typical angioma arteriale racemosum, inoperable because of its vascularity; decompression; diminution of subjective symptoms following decompression and X-ray treatment. Clearly audible auscultatory bruit over tumour; increase in intensity of bruit during visual effort.*

[1] Further clinical details concerning this case, with full discussion of the pathology of this group of rare and interesting tumours, is given by Cushing and Bailey in their monograph, "Tumors arising from Blood-vessels of the Brain: Angiomatous Malformations and Hæmangioblastomas." Springfield: Thomas, 1928 (in press).

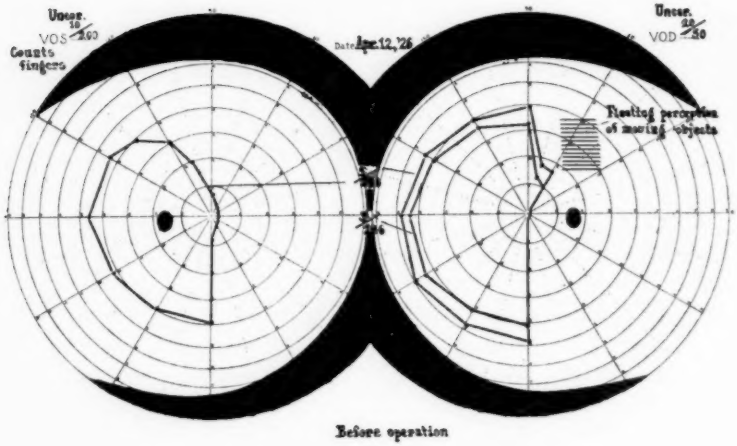

FIG. 1A.

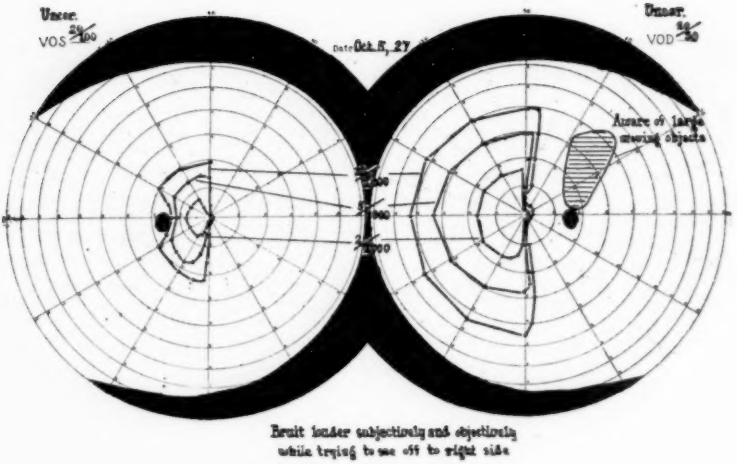
Uncor.
VOS 20/200
Date Oct. 8, '27
Uncor.
VOD 20/30
Aware of large moving objects
Bruit louder subjectively and objectively while trying to see off to right side

FIG. 1B.

FIG. 1.—Visual fields, (A) before, and (B) one and a half years after, operation, showing right homonymous hemianopsia with partial sparing of macula. The hemianopsia was incomplete, since in the upper temporal quadrant of his right eye the patient was dimly aware of moving objects. It was when attempting to perceive moving objects to his blind side that the bruit in his left occipital region was most noticeably augmented.

Walter K., a single German-American sailor, aged 26, was admitted April 12, 1926, because of headache and failure of vision. The patient stated that for seven years he had had increasingly severe pain in his left temporal region which, however, had diminished a few months before entry. For five years he had had failing vision, the left eye having been reduced to almost complete blindness, and he had noticed for several months that he could not see to his right side. During the previous six months he had been conscious of a humming noise referred to his left ear. There had been no deafness, dizziness, ataxia or vomiting, and no weakness of any of the extremities.

Physical examination revealed a loud, coarse systolic bruit over the left occipital region, right homonymous hemianopsia with sparing of the macula (fig. 1), left exophthalmus with slight pulsation, bilateral choked disc with evidence of extensive secondary optic atrophy on the left side and early secondary atrophy on the right. There were no other significant neurological findings, except that the pulsation of the left temporal artery was more forceful than of the right. The deep reflexes were equal and active, and there were no cranial nerve palsies. X-ray of the skull (fig. 2) disclosed an area of increased vascularity over the left occipital lobe with slight erosion of the bone in this area. There was also a moderate increase in convolutional markings suggestive of increased intracranial pressure.

At *operation*, on April 23, 1926, Dr. Cushing, in anticipation of encountering a highly vascular tumour, carried out first a bilateral ligation of the external carotid arteries. On turning down a left occipital bone flap, a large, angry-looking angioma arteriale racemosum of the left occipital lobe was disclosed which extensively involved the visual cortex. The hæmorrhage occasioned by the bone flap was so excessive that the operation had to be abandoned without touching the tumour. A decompression, however, was made. The patient was discharged on May 16 after a normal post-operative recovery, with greatly improved vision, diminution of left exophthalmus and freedom from occipital pain, but the bruit still persisted. After discharge from the hospital he was given two series of deep X-ray treatments, which produced a marked diminution in the intensity of the cerebral bruit. The patient was conscious of this himself, and it was evident to those who examined him. His vision also continued to improve.

Second entry.—The patient re-entered the hospital September 27, 1927, at Dr. Cushing's request, for further observation and possible operation. Examination at this time showed a well-developed man in excellent physical condition, with well-healed bilateral scars on his neck and a pulsating post-operative defect in his left occipital region. The bruit was still audible over the defect, but it had apparently diminished in intensity. There was bilateral secondary atrophy, more marked left than right, right homonymous hemianopsia, complete for resting but incomplete for moving objects, and a concentrically-constricted left temporal field (see fig. 1B). Visual acuity was $\frac{20}{100}$ left, $\frac{20}{30}$ right, uncorrected. His fundi showed tortuous veins and it was observed in his left fundus that, though the veins did not pulsate, there was very little difference in

colour between arteries and veins. On compressing his jugulars the retinal veins could be made to pulsate with ease: the difference in colour between arteries and veins then became somewhat greater. During jugular compression his left temple swelled while his right did not. There were no other significant neurological signs.

Observations on the bruit.—Several days after entry, while testing the patient's fields, he remarked that the noise in the back of his head increased in intensity when he was using his eyes. He said that he

FIG. 2.—X-ray photograph of skull (left) prior to operation, showing area of bony rarefaction in left occipital region overlying the angioma.

had often noticed this during the past several years, but had "never thought much of it." On listening to the bruit, it was obvious that it was much louder than when first examined on the day of entry. Subsequent observations were made during the following week, and it was not difficult to convince ourselves that when the patient suddenly began to use his eyes after a prolonged period of rest in a dark room,

there was a prompt and noticeable increase in the intensity of his bruit. The increase was detectable within twenty to thirty seconds, and if he was permitted to use his eyes for one to one and a half minutes, and then directed to close his eyes, the bruit would continue at heightened intensity for nearly a minute and then gradually subside. The patient was cautioned not to make his muscles tense during the time when his eyes were being tested, and we believe that the only significant additional muscular effort was that of opening and closing his eyes. Simultaneous observations of his blood-pressure during the time that his eyes were being tested gave inconstant results. On one

FIG. 3.—Patient three weeks after operation, showing the region explored. The arrow indicates the point of maximum intensity of the bruit. This overlies the region of greatest vascularity of the angioma.

occasion, during a long session in which his fields were being tested, there was a rise of five to ten points in his systolic pressure (120-125-130). Frequently, however, there was an increase in the intensity of his bruit without any concomitant rise of blood-pressure, and there was no change in pulse-rate. Activity of his other sense organs, moreover, had no effect upon his bruit. Thus, smelling tobacco or vanilla did not influence it, straining to hear the ticking of a distant watch produced no effect, and ordinary quiet conversation was without demonstrable influence. We believe, therefore, that the effect is due to a genuine increase in the vascularity of the region about his left occipital lobe.

As stethoscopic observations on the augmentation of the bruit during visual activity are open to the objections associated with any subjective impression, further evidence was secured by recording the bruit photographically with a microphone and a string galvanometer. The patient was allowed to lie on his stomach in a comfortable position, with his chin resting on the edge of a chaise-longue in such a way that he could close his eyes and open them to read a newspaper lying on the floor. He was permitted to rest in this position in a completely darkened room for five to ten minutes before observation. Records

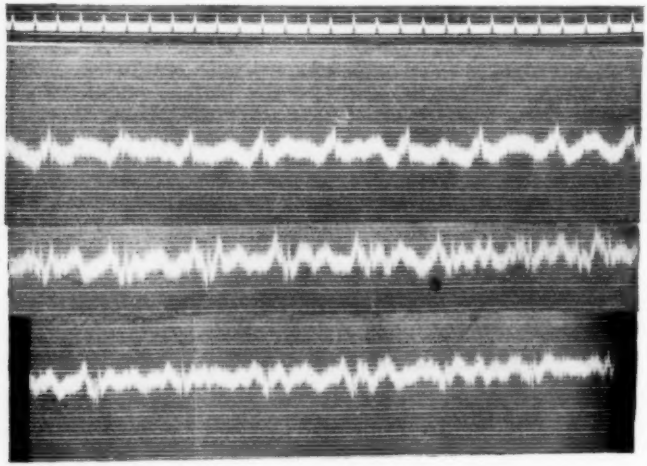

FIG. 4.—Typical electrophonograms of bruit. A, after ten minutes' rest in a darkened room; B, after two minutes' reading of small print illuminated by a single 40-watt tungsten bulb at 5 feet; C, three minutes later, after two and a half minutes' rest in darkened room. Note increased size of main deflections in B and the greater number of secondary deflections. (Telephone transmitter placed directly over point of maximum intensity of bruit on shaved scalp: transmitter in series with Einthoven string galvanometer.) Time above: 0·2 sec.

were then taken of the magnitude of the excursions set up by the bruit, and then the light was turned on the newspaper in front of him and he proceeded to read the smallest type which he was able to see, having been cautioned beforehand not to use his lips or to move in any way. The microphone was placed directly on the back of his head at the point of maximum intensity of the bruit, as determined previously by the use of a bell stethoscope. His head was shaved over the area so as to exclude extraneous noises, such as come from the crinkling of the hair. In one or two records in which he inadvertently spoke, the

voice was transmitted so markedly that the string was thrown into a veritable paroxysm of vibration. When the microphone was placed on other regions of his head the string was absolutely quiet.

Repeated observations with this technique showed that within twenty to thirty seconds after the patient began to use his eyes there was a noticeable increase in the intensity of the bruit. This continued and reached a maximum at the end of one to two minutes (fig. 4). If at this time the lights were put out, the bruit continued very loud and coarse, as judged by the string records, for nearly a minute after the lights were turned off; then it gradually subsided, and at the end of two minutes had returned practically to the resting level (see fig. 4). This observation was repeatedly confirmed.

Critics may object that the magnitude of the sound over an aneurysmal tumour is not an adequate index of circulatory activity. Constriction, for instance, of the arteriovenous communications might lead to an increase in the bruit without an increase of blood-flow. But that this is not the case is evident from the fact that the patient's decompressed area immediately over the angioma, though soft at the beginning of an observation, usually bulged markedly after he had been using his eyes for some time, the position of his body remaining unchanged. It is interesting, also, that jugular compression causes an immediate cessation of bruit. When the jugulars were released the bruit returned with increased intensity for a few seconds and then gradually subsided to normal.

After the patient was discharged (October 14, 1927), he was observed every two to three weeks for five months, during which period he had a series of X-ray treatments directed toward his tumour. At first the treatment seemed to have little effect upon the resting intensity of his bruit, but gradually, after about three to four months, a noticeable diminution occurred. When the patient was last seen (February 28, 1928), the following note concerning his bruit was made on his hospital record :—

"Patient feels since last three X-ray treatments that his bruit has diminished almost to the vanishing point. He now is conscious of it only at night when he lies down with his head on the pillow, but never seems to be aware of it during the day unless he performs some vigorous exercise. Since we showed him that jugular compression caused the bruit to disappear, he frequently checks the sound himself when he thinks it is coming. If present, he can shut it off readily by squeezing his own neck, and is then immediately conscious of its disappearance.

"When patient first entered the hospital this afternoon, the bruit was completely inaudible. Moreover, the decompressed area at his left occipital pole was soft and appeared even slightly sucked in. On previous visits the decompression has always been slightly tense with a moderate bulge. During the forty-five minutes that patient waited, I talked with him the greater part of the time and listened to his bruit, as did also Dr. Bailey, but neither of us was able to detect anything but a most distant and scarcely recognizable sound. His fields were taken at 5 o'clock, and five minutes later the bruit was moderately loud and clearly audible. Patient was conscious of its reappearance as we were taking his fields, especially when trying to see to his right homonymous side. The decompression also became somewhat more full. Dr. Bailey listened to the bruit after the fields were taken, and was quite astonished at the extent of its augmentation. Slight bilateral jugular compression caused the bruit to disappear immediately, and firm compression of his neck (sufficient to abolish his temporal pulse) did not lead to its reappearance. During firm jugular compression the left eye, which is still slightly exophthalmic, pulsated just perceptibly. Jugular compression gave the patient rather a severe headache, so we did not pursue the observation further. The quality of the bruit is altered since it was last heard, it being now low-pitched and machinery-like in quality, whereas before it was high with more over-tones.

"*Visual fields.*—His right homonymous defect is now complete, and appears to have diminished somewhat during the course of X-ray treatments. I fancy that the shrinking up of the blood-vessels in his left visual cortex may have impaired what little functional visual cortex may have remained on that side. It seems extraordinary, however, that the patient still has undoubted vasomotor response on that side during visual effort."

"The *fundi* are essentially unchanged, except for the fact that the veins appear less full than when previously examined. There is marked secondary atrophy of the left and slight secondary pallor of his right disc. The difference in colour between the arteries and veins of the left eye appears to be more marked than before. In other words, this would appear to indicate that there is less arteriovenous communication in his cerebral vessels than previously."

He had further X-ray treatments after this visit, and on June 8, 1928, he wrote: "I have no more noise in my head, even when I use my eyes for some length of time." Evidently the prolonged X-ray therapy eventually produced complete thrombosis of the angiomatous vessels.

Interpretation.

In considering the interpretation of the foregoing observations, we may mention the following additional facts. Careful observations of patient's blood-pressure during visual tests showed that there was no significant increase in his systolic pressure. On one occasion, when a large number of observers were in the room and the patient remarked

that he was getting worked up by having so much done to him, a rise of ten points in his systolic pressure was observed. On this occasion the patient was conscious that his bruit had increased, and he said that when he gets worked up in this way it is apt to stay very loud for ten to fifteen minutes, and this in fact proved to be the case by observation of the intensity of the sounds by auscultation. However, when the patient merely opened his eyes and attempted to read the eye-testing chart, there were no emotional stimuli, and he was cautioned not to move or speak during the period of observation. Under these circumstances there was no elevation whatsoever in his systolic blood-pressure, but there was a noticeable increase in the intensity of the bruit. We gained the impression that it was the effort of trying to discern objects which were just at the limit of his acuity which brought on the increase in intensity of the bruit. Merely shining light into his eyes when he was making no mental effort did not appear to do it. Moreover, the bruit increased very markedly when he attempted to read a paper in poor light, so that we believe that the light *per se* had very little influence upon the results. As to whether the effort of accommodating or moving his eyes was involved in the response, we are unable to say. The effort, in other words, of attempting to discern poorly-lighted or small objects appears to be the most potent stimulus.

It is also significant that auditory and olfactory stimuli did not increase the intensity of the bruit; that is, the response is connected with a process localized in the region of the vascular tumour. This, be it noted, is entirely in harmony with Cobb and Talbot's experimental observations upon the increased vascularity of the olfactory bulbs following olfactory stimuli. They were unable to detect any increase in vascularity in other portions of the brain.

In conclusion, it would seem evident that the observation just described strongly supports the view that localized increase in vascularity of the brain occurs under appropriate sensory stimulation, or, more specifically, it is probable that visual activity in man is associated with an increase in the vascularity of the occipital lobes.

Summary.

A case is described of a man in whom there was a circumscribed angioma arteriale racemosum of the left occipital visual cortex which had produced an incomplete right homonymous hemianopsia. Associated with the tumour was a well-marked auscultatory bruit. When

the patient was at rest with his eyes closed the bruit was distant and weak. When the patient used his eyes for reading, or attempted to perceive objects to his blind side without otherwise exerting himself, a very marked increase occurred in the bruit, detectable both by auscultation and by electrophonograms. Other types of mental effort, such as straining to hear the tick of a distant watch or various forms of olfactory stimulation, had no influence upon the bruit. It would appear that visual effort was associated in this case with increased vascularization of the occipital cortex.

BIBLIOGRAPHY.

BECKER, F. C., and OLSEN, O. "Metabolism and Mental Work," *Skand. Arch. Physiol.*, 1914, **31**, 81-197.

BENEDICT, F. G., and CARPENTER, T. M. "The Influence of Muscular and Mental Work on Metabolism, and the Efficiency of the Human Body as a Machine," *Bull. No. 208. U.S. Dept. of Agriculture*, 1909. 100 pp.

COBB, S., and TALBOT, J. H. "Studies in Cerebral Circulation. No. 2. A Quantitative Study of Cerebral Capillaries," *Trans Assoc. Amer. Physicians*, 1927, **42**, 255-262.

CRAIGIE, E. H. "On the Relative Vascularity of Various Parts of the Central Nervous System of the Albino Rat," *Journ. Comp. Neurol.*, 1920, **31**, 429-464.

Idem. "The Vascularity of the Cerebral Cortex of the Albino Rat," *ibid.*, 1921, **33**, 193-212.

Idem. "Changes in Vascularity in the Brain-stem and Cerebellum of the Albino Rat between Birth and Maturity," *ibid.*, 1924, **38**, 27-48.

Idem. "Post-natal Changes in Vascularity in the Cerebral Cortex of the Male Albino Rat," *ibid.*, 1925, **39**, 301-324.

Idem. "The Vascularity of the Vagus Nuclei and of the Adjacent Reticular Formation in the Albino Rat," *ibid.*, 1926, **42**, 57-68.

Idem. "Notes on the Vascular Supply in the Brain of a Holocephalian, Hydrolagus (Chimæra) Colliei," *ibid.*, 1927, **43**, 193-200.

CUSHING, H., and BAILEY, P. "Tumors of the Brain arising from its Blood-vessels, Angiomatous Malformations and Hæmangioblastomas." Springfield: Thomas, 1928.

DAY, MILDRED E. "The Influence of Mental Activities upon Vascular Processes," *Journ. Comp. Psychol.*, 1923, **3**, 333-378.

GILLESPIE, R. D. "The Relative Influence of Mental and Muscular Work on the Pulse-rate and Blood-pressure," *Journ. Physiol.*, 1924, **58**, 425-532.

v. LIEBERMANN, L. "Energiebedarf und mechanisches Aequivalent der geistigen Arbeit," *Biochem. Zeitschr.*, 1926, **173**, 181-189; Physiol. Abstr., 1926, vol. xi, p. 370.

PFEIFFER, R. A. "Die Angioarchitektonik der Grosshirnrinde." Berlin: Julius Springer, 1928. 157 pp.

CHRONIC PROGRESSIVE EXTERNAL OPHTHALMOPLEGIA.[1]

Report of a Case with Necropsy.

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Different forms of external ophthalmoplegia are well known, but in this communication we shall describe an unusual clinical case, the only one, we believe, with necropsy, belonging to a group described in the literature as "chronic, progressive, external ophthalmoplegia."

Wilbrand and Saenger [15] collected thirty-two cases of this form of ophthalmoplegia and, because of the following clinical characteristics, they regarded it as a distinct clinical entity :—

"Bilateral, slowly-progressive paralysis of the external muscles of the eyes develops without any other signs of disease. Years may elapse between the development of the first symptom and the development of complete ophthalmoplegia. The onset is gradual, usually beginning in childhood, seldom in adult life. The rate of progression is variable, but it generally ends in complete external ophthalmoplegia. Ptosis may be the first sign of the disease and may, for a considerable period of time, be the only one. After the ocular muscles become affected, diplopia may be complained of, but this symptom is infrequently noted because of the extremely slow progress of the paralysis, and because it is generally symmetrical. The health of the patient is not affected. It is a striking feature of the affection that no other signs or symptoms develop indicating implication of other organs or other structures of the nervous system."

McMullen and Hines [10] reported three personal observations. (One of the cases, however, showed signs of disease of the central

[1] Read before the meeting of the American Neurological Association, Washington, D.C. May 5, 1928.

nervous system, confirmed at a later examination, so that it can be excluded from the group.)

Discussing the literature, they refer to cases reported since Wilbrand and Saenger's article by Beaumont (twelve cases) and Atland. The characteristics of Beaumont's cases were: (1) Familial; (2) never congenital; (3) slowly progressive; (4) never fatal.

In Atland's [1] case the trouble developed, at the age of 22, in the right upper lid, and at 40 the left upper lid became affected. When seen at the age of 51 the ptosis of the right eyelid was complete, that of the left incomplete, and both globes were immovable.

In discussing the various forms of hereditary ocular paralysis, Collins [5] quoted Gowers' own statement regarding his well-known theory of "abiotrophies," and pointed out that in chronic progressive ophthalmoplegia all the orbital striated muscles became paralysed, but the unstriated intra-ocular muscles invariably remained unaffected, and he emphasized the fact that many of the cases belonging to this group had been watched for long periods of time, and that not one of them had ever developed additional symptoms attributable to the nervous system. For this reason he alluded to the apparent resemblance of the paralysis of these cases to an isolated form of bilateral ptosis described by Fuchs [7] in 1890, and which he thought were cases of primary myopathy. Collins suggested, because of this apparently strong circumstantial evidence, that chronic progressive bilateral ophthalmoplegia might be, in reality, another limited form of primary myopathy and not, therefore, dependent upon alteration of the nervous system.

Wilbrand and Saenger [15] regarded this condition as a disease of the ocular nuclei, while Brouwer [3] thought it was dependent upon alterations of the nerve trunks innervating the extra-ocular muscles. Wilbrand and Saenger, as well as Collins, reviewed the literature of the subject and stated that there had never been a post-mortem examination reported. Since their descriptions were published in the years 1920 and 1922 respectively, a number of clinical cases have been recorded, but we have been unable to find the record of a single necropsy.

The case which we have to record here was carefully studied during the lifetime of the patient by both of us. Only the brain was obtained for examination. The third, fourth and sixth cranial nerves and the optic nerves were cut in cross and in longitudinal sections. The brain-stem was cut in serial sections, and every tenth section was stained with haemalum and acid fuchsin, and with the Weigert and Nissl methods;

additional sections were stained with toluidin blue and the van Gieson method. Unfortunately, the ocular muscles were not obtained for examination.

Mrs. W. H. C. was first examined in January, 1924, at the age of 81, and was under observation until her death at the age of 84. It was stated by the patient, and also by her daughters, that the right eyelid had begun to droop at the age of 43 (a photograph of the patient was shown to us, taken at the age of 30, in which ptosis was not revealed, but another photograph, taken at the age of 48, showed right-sided ptosis), and soon after this the left lid was similarly affected. It is not known positively what time had elapsed after the onset of ptosis, or even whether the ptosis had preceded the completion of external

FIG. 1.—Patient, aged 81, showing bilateral ptosis. (Page 3 of paper.)

ophthalmoplegia, for it was not discovered by one of us (Dr. Langdon) until fully developed, when the patient had reached the age of 75. The general health of the patient at that time and subsequently had been very good. She had had no evidence of illness of any kind. Her parents had been normal, and her near living relations and three daughters were in perfect health and, on inquiry, it was stated that no other members of the family had had a similar disease.

Examination revealed complete ptosis of each eyelid; the visual axes were slightly divergent, the pupils measured 3 mm. on each side and reacted promptly to light. The power of accommodation was very feeble, but not entirely lost. The two eyeballs appeared immobile, but on voluntary effort an extremely slight movement of each eyeball, when rotation was attempted in any direction, could be detected. When both eyelids were held open by the examiner

diplopia developed, but when only one eyelid was held open at a time by adhesive plaster attached to the brow, the patient got on quite comfortably. There were some changes in the lens in each eye; the rest of the media were clear. The retinal arteries were irregular, with some indentation of the underlying veins. The discs were well coloured with clear margins. The fundi otherwise were in good condition. The corrected vision of the right eye was $\frac{6}{60}$ and of the left eye $\frac{6}{6}$.

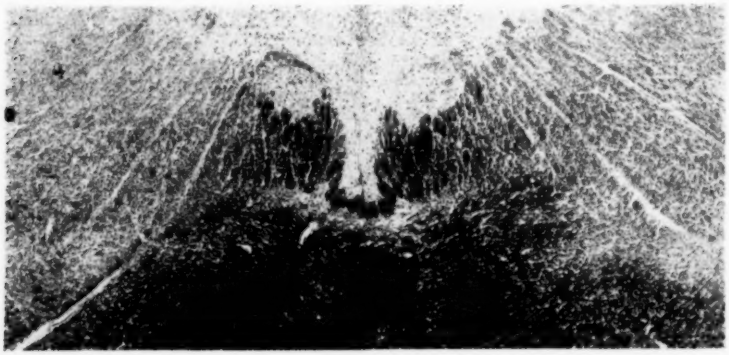

FIG. 2.—Normal fourth nerve nuclei for purposes of comparison with fig. 3.

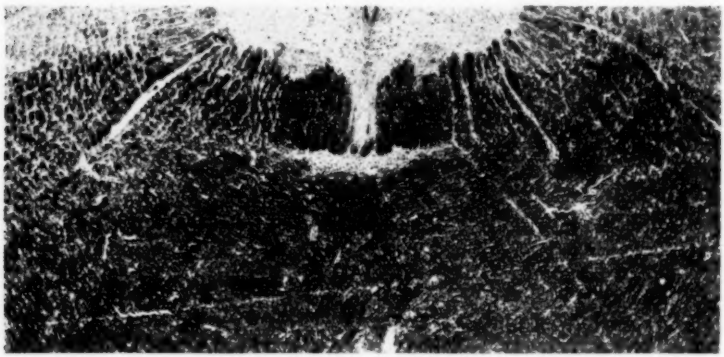

FIG. 3. -Showing pathological fourth nerve nuclei. The diameter of the nuclear groups appeared shorter than those of the normal nuclei of the control sections.

There was, therefore, very nearly complete loss of all extra-ocular muscular power, with preservation of the reactions of each pupil to light. Movements of convergence were practically impossible. The functions of the other cranial nerves were carefully tested and were found normal, as well as the muscles innervated by them. The muscular power of the upper limbs was entirely normal, and the biceps and triceps reflexes were normal. There was no

muscular atrophy. The muscular power of the lower limbs was equal and normal, the patellar and Achilles reflexes were normal, and the gait and station were natural. No additional evidence of disease could be discovered.

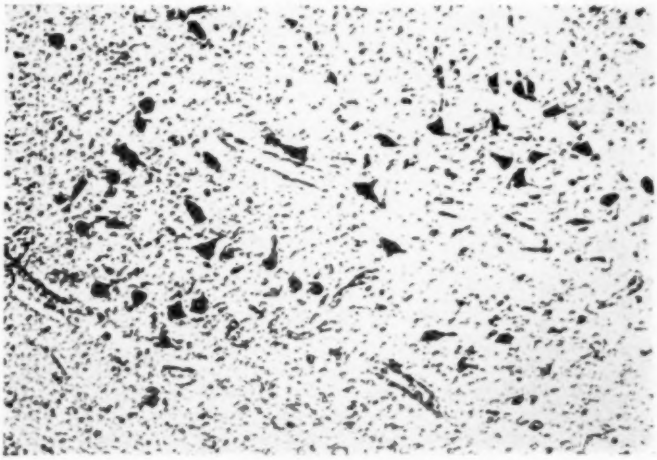

FIG. 4.—Cells of the sixth nerve nucleus from a normal case, for the purpose of comparison with fig. 5.

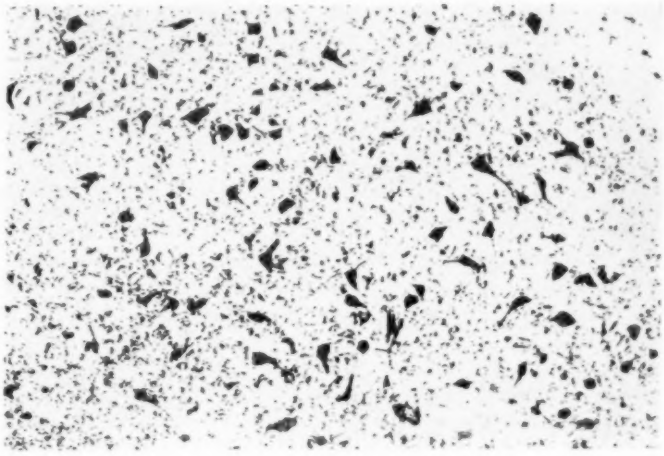

FIG. 5.—Cells of the pathological sixth nerve nucleus, showing the variations in size.

There was a moderate degree of general arterio-sclerosis, no greater, however, than might be expected in a normal woman aged 81.

The patient died of pneumonia at the age of 84 without having developed additional symptoms.

Necropsy report.—The sixth nerve nuclei were easily recognized. The cells of each nucleus were well stained, and chromatolysis was very slight when compared with the cells of a normal nucleus in sections made from a young adult for the purpose of control. The nerve cells were slightly diminished in number and presented definite variations in size and, to some extent, in shape. At least one-third or one-half their number were distinctly smaller in diameter than the others. Similar appearances were not observed in the control sections. The axis cylinders stained normally in Weigert sections. The bundles of fibres composing the root of the sixth nerves in their course through the pons appeared smaller in diameter and less numerous than those in the corresponding normal sections.

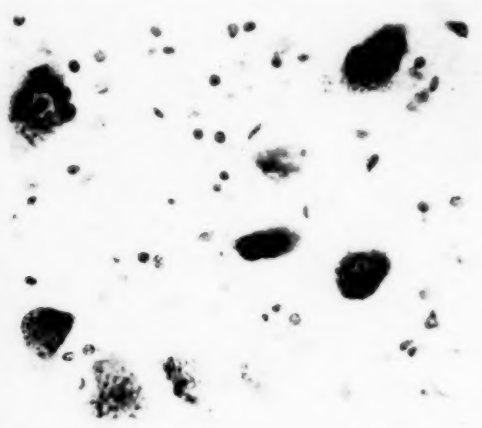

FIG. 6.—Cells of the oculomotor nucleus, one showing evidences of chromatolysis.

The cells of the trochlear nuclei presented the same appearances. The diameters of the whole nuclear groups appeared shorter than those of the normal nuclei of the control sections, and the bundles of the fourth nerve were smaller.

The cells of the oculo-motor nuclei of each side were slightly diminished in number, especially in the lateral cell groups in the sections of the middle and more caudal levels. In the sections from the more proximal levels, this diminution in number of cells was not so apparent. In no section, however, were the differences in the number of cells composing the different groups very striking, yet in the normal control sections the corresponding cells appeared more uniformly distributed and more numerous than in the pathological sections. Variations in the size of the cells were observed, but it was difficult

to determine whether these variations were much greater than similar differences in the size of the cells seen in normal specimens. Some cells had undergone chromatolysis, but this was not a conspicuous feature; many of the cells were deeply pigmented. The cells composing the nuclei of Darkschewitsch were normal in size and shape, and did not appear to be distinctly diminished in numbers, but contained much more pigment than was observed in cells of the oculo-motor group. The cells occupying the median position, corresponding to Perlia's nucleus, appeared normal.

The cells of the Edinger-Westphal nuclei were numerous, well-shaped, uniform in size, with clear nuclei and without chromatolysis, and were conspicuously free from pigmentation.

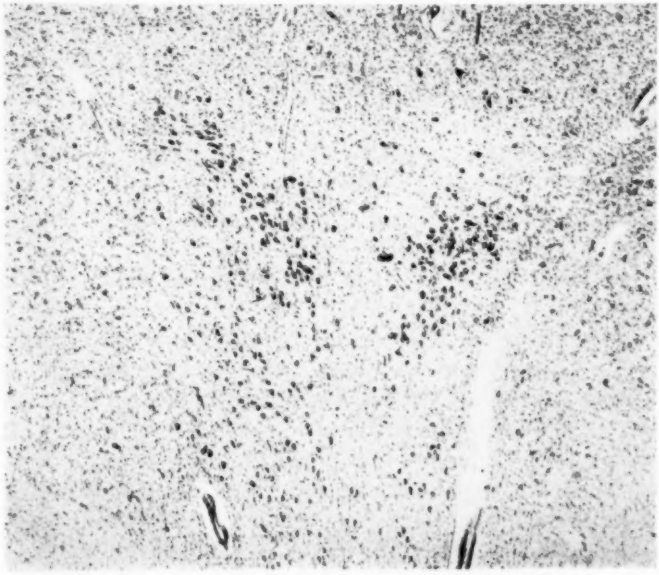

FIG. 7.—Showing preservation of the cells of the Edinger-Westphal nuclei.

The fibres of the oculo-motor nerves stained well by Weigert's method, but were much less conspicuous than in normal sections, and the bundles appeared smaller in diameter than normal. The internuclear nerve fibres (fibræ rectæ) were normal in appearance. There was no evidence of nerve degeneration elsewhere in any of the Weigert sections, nor was there any evidence of inflammatory reactions.

Sections of the third, fourth and sixth nerve trunks stained fairly well with acid fuchsin and Weigert's method, but these again appeared smaller in diameter than corresponding control specimens. The optic nerves were normal.

Comment.—We are fully aware of the fact that cells composing some nuclear groups may normally present variations in size. In the oculomotor nuclei differences in the size of the cells is well known, but pronounced differences in the size of the fourth and sixth nuclear cells are unusual and must be abnormal. According to most authorities, including Winkler [16], the cells of the fourth and sixth nuclei are more uniform in size than those of the third nuclei. Smallness of the ocular nerves was apparent, even to the naked eye, not only in their intramedullary course, but also the extramedullary nerve trunks. The other cranial nerves did not appear so small in comparison.

Senility does not produce distinct alterations in the size of the nerve cells, though Donaldson [6] has observed a shrinkage of the whole brain, determined by weighing, owing to old age alone. We know of no evidence that cessation of muscular contraction alone for a long period of time, as occurred in the extra-ocular muscles of this case, is capable of producing shrinkage of the nerve trunks innervating the muscles so affected, so we are forced to the conclusion that the alterations we have found were sufficient to explain even the extreme degree of ophthalmoplegia with which they were associated.

We wish to point out the striking resemblance of these changes to those found by Greenfield and Stern [8] and others in cases of progressive spinal muscular atrophy of childhood of the Werdnig-Hoffmann type, for we believe the case we have described must be regarded as a similar form of chronic neuron degeneration, though the alterations were entirely limited to the ocular neurons, and we think it is probably the same pathological process that produces progressive spinal muscular atrophy when the spinal neurons are affected. Why some of these cases of ophthalmoplegia seem to be hereditary or familial in character, as were Beaumont's cases, or develop sporadically in early and but seldom in later life, might be due to the same factors, whatever they may be, that determine the time and character of onset of the symptoms in spinal muscular atrophy.

The extra-ocular muscles were not examined, but had they been we are certain that they would have been found severely atrophied, for it is inconceivable that such severe neuron paralysis which had persisted for so many years would not have produced very decided muscular atrophy.

Collins examined a piece of excised muscle from his case and found it atrophic, but it was not examined microscopically.

Siemerling [13] reported a case of left-sided congenital ptosis, with

necropsy. The movements of the eyeballs were normal and the reflex pupillary movements were preserved. He found degeneration of the cells of the oculo-motor nucleus in the more proximal levels. The right oculo-motor nucleus was normal. He also stated that the intramedullary oculo-motor nerve bundles, as well as the fibres of the extramedullary oculo-motor nerve trunk on the affected side, were much thinner than normal.

Fuchs reported, in 1890, five cases which have already been referred to by Collins, in which bilateral ptosis was the only symptom of disease. In three of these the condition was acquired, and in two it was hereditary. The muscles of the eyelids were extremely wasted, and in a portion of these atrophic muscles excised for microscopical examination the fibres appeared much thinner than normal, the nuclei were increased in numbers and there was pigmentary degeneration inside the sarcolemma, but no fatty degeneration was found. The connective tissue between the muscle fibres was increased in amount. Fuchs discussed at length the difference in the appearance of muscles atrophic as the result of neuronic disease, and of that due to primary muscular atrophy, and emphasized that in the latter condition hypertrophy of some fibres is generally found. Though admitting that, in his case, because of the small microscopic specimens, differentiation was extremely difficult, he seemed to believe that it was in reality a primary myopathic disease.

Judging from Fuch's description, we think his cases of isolated ptosis must have been the result of primary myopathy, an entirely different disease from the case we have observed, and we have only referred to them for the purpose of emphasizing the important differences in the character of muscular atrophy. The muscles of the eyelids of Fuchs' cases were extremely wasted. In our patient the muscles of the eyelids were not atrophic, and obvious muscular atrophy has not been recorded in other cases of chronic progressive ophthalmoplegia that we have alluded to.

Implication of the extra-ocular muscles, exclusive of the levatores palpebræ, has rarely been observed in progressive muscular dystrophy (primary myopathy). Wilbrand and Saenger [15] refer to only two cases, one reported by Gowers, and one by Winkler and von der Weyde. Oppenheim [11] says that ocular paralysis has been observed very exceptionally in progressive muscular dystrophy, and refers to a few cases reported in the literature. Yuma Sunaga [17], in an article on the trophic innervation of the extra-ocular muscles in relation to experi-

mental and pathological studies on progressive muscular atrophy, says that he has had the opportunity of examining the eye muscles in two cases of progressive muscular dystrophy. Macroscopically, the external recti and obliques presented no alterations, but microscopically he found the characteristic picture of muscular dystrophy. After extirpation of the ciliary ganglion in dogs, he found alterations of the external eye muscles (recti and oblique) that resembled closely those of muscular dystrophy, and attributes these lesions to the cutting off of trophic innervation from the sympathetic nerves. He refers to the investigations of his colleague, Ken Kuré, and others.

Ptosis with paralysis of the extra-ocular muscles is well known in myasthenia gravis, a condition affecting striated muscles primarily, but the characteristic of this form of paralysis is the tendency to recover muscular function after rest, and rapid exhaustion of function from prolonged effort. Yet Collier [4] asserts that it is well known that the paralysis of myasthenia gravis may become complete and permanent. In our case there were no symptoms suggesting myasthenia gravis.

Spiller says [14], in discussing oculo-gyrations and the lesion causing complete bilateral ophthalmoplegia: "I believe that, when the central pathway of cortico-nuclear oculo-gyration is paralysed above or in the nucleus of the nerve to the affected internal rectus, the function of this muscle in convergence will disappear or become much impaired, as it did in the case I now report. When the break occurs in these fibres above this nucleus, no impulses can pass into this nucleus for either form of function of the internal rectus, i.e., for oculo-gyration or for convergence; but, when the break occurs in the posterior longitudinal bundle, and therefore below the nucleus of the nerve to the internal rectus, the function of the internal rectus muscle in convergence may be preserved, as it has no relation to the abducens nerve, but oculo-gyration demanding the function of this muscle in association with the function of the hetero-lateral external rectus will be lost. So far as I know, this diagnostic distinction of a lesion above the nucleus of the nerve to the internal rectus, as compared with one in the posterior longitudinal bundle below this nucleus as of value in localization, has not been described, and it applied to the lesion above the nucleus only when it is near the nucleus.

"Complete ophthalmoplegia, implicating all the nerves supplying the eyeballs, has been explained usually as the result of inflammatory lesions of all the ocular nuclei, but this explanation, when all other cranial nerves entirely escape, has seemed to me unsatisfactory,

especially as bilateral complete ophthalmoplegia has been repeatedly observed without other nerve lesions. I believe that when a lesion destroys the nuclei of the trochlearis and oculo-motorius nerves bilaterally, which a comparatively small lesion may readily do as these nuclei are very near together, it must destroy the connections in the posterior longitudinal bundles between the nuclei of the internal recti and those of the external recti, and consequently paralysis of the external recti muscles will result without any lesion of the abducens nerves or their nuclei. The movements of the two eyeballs are intimately associated, and a lesion of the central pathway of cortico-nuclear oculo-gyration near the nuclei affects the movements of both eyeballs."

Collier has described how a lesion situated above the oculo-motor nucleus is capable of producing complete ophthalmoplegia, but he points out that when ophthalmoplegia occurs from a lesion in this situation the eyelid is retracted and ptosis will not develop. In his case there was a hæmorrhage in the region of the posterior commissure, and retraction of the eyelid was observed. The oculo-motor nuclei were not implicated by the lesion; the paralysis, he thought, had been produced by destruction of the efferent ocular cerebral fibres in their course downward from the brain, before they had reached the level of the oculo-motor nuclei to connect with them.

In our case, and in all similar cases alluded to here, the pupillary reflexes to light especially, and to a less degree on accommodation, were preserved, and in our case the Edinger-Westphal nuclei were intact. This fact would appear to support the view so generally held that the function of the Edinger-Westphal nuclei is essentially for the control of the pupillary movements.

Brouwer has paid particular attention to this problem. He described a case of ophthalmoplegia in which the oculo-motor nerve had been compressed by an aneurysm of the carotid artery, but with the preservation of the pupillary reflexes, yet the cells of the Edinger-Westphal nucleus presented some alterations. He attributed the cell changes to retrograde effects of compression exerted upon the oculo-motor nerve. In discussing the literature of the subject, he referred to the cases of Cassirer, the work of Tschuda, Bernheimer, and others, and said he had been unable to find a single case recorded in the literature in which destruction of the Edinger-Westphal nucleus had occurred with preservation of the pupillary reflexes to light and on accommodation. From his studies of the literature and his own investigations in comparative and pathological anatomy, he concluded that the Edinger-Westphal

nucleus was certainly the sympathetic part of the oculo-motor nucleus, and referred to the fact that Jacobsohn had given it the name of "nucleus sympathicus nervi oculomotorii."

Wilbrand and Saenger, after having referred to the work of others, point out that the Edinger-Westphal nuclei lie so close to other cell groups of the oculo-motor nuclei that functional differentiation by experimental methods alone is exceedingly difficult. They quote the case of Gruenstein and Georgieff [9], in which there had been bilateral ophthalmoplegia with preservation of the pupillary reflexes. Microscopically, these authors found two lesions in the peduncles destroying most of the cells of the oculo-motor nuclei, while the Edinger-Westphal nuclei were preserved for the most part, only a very few of the cells in the posterior portion of one of the group were implicated in the lesion, which was a tubercle. They regarded this observation as important evidence that the Edinger-Westphal nucleus had to do with the pupillary reactions.

Leslie Paton and Ida Mann [12] studied the development of the third nerve nucleus in its bearing on the Argyll Robertson pupil, and concluded that the view that the median nucleus of Perlia is concerned with convergence, and the Edinger-Westphal nucleus with pupil movements, is supported by the study of their development in man, since the time of appearance of the various parts of the nucleus appears to be correlated with the development of the mechanism of their respective functions.

It is significant that Brouwer and Winkler both quote the work of Cajal, who said that although he had been able to demonstrate the Edinger-Westphal nucleus in the cat, mouse and dog by silver methods of staining, he had been unable to follow their axis cylinders into the oculo-motor nerve trunks, and consequently suspected it was not really part of the oculo-motor nucleus. It appears, therefore, that the cells of the Edinger-Westphal nucleus must represent a separate neuron system, and for that reason it was not affected in our case, thus explaining the preservation of the pupillary reflexes.

The most recent and most convincing work on the subject is that of Winkler. He says that the cells of the Edinger-Westphal nuclei do not send fibres to the oculo-motor nerve-roots, and consequently should not be considered as parts of the oculo-motor nuclei. By extirpation of the ciliary ganglion in cats, and also after section of the oculo-motor nerve, he found no effect whatsoever on the cells of the Edinger-Westphal nucleus. He points out that this result is diametrically opposed to Bernheimer's results, for Bernheimer believed he had been able to

establish that the Edinger-Westphal nucleus disappeared on the operated side after extirpation af the ciliary ganglion. Winkler thinks it probable that Bernheimer had been misled, because the Edinger-Westphal nucleus is inconstant and not easily recognized in some animals, and that he might have operated upon an animal in which, by chance, the nucleus was very poorly developed.

Winkler regards the Edinger-Westphal nuclei and also Darkschewitsch's nuclei as separate from the oculo-motor nuclei, and thinks they are intercalated groups of cells which have to do with the synergic movements of the eye, the latter representing part of the mechanism for the control of the upward, associated movements of the eyeballs. He describes the Edinger-Westphal nucleus as situated among the fibræ rectæ and surrounded by them, the fibræ rectæ passing through the grey matter between the proximal part of the main lateral groups of the oculo-motor cells. The Edinger-Westphal nucleus in the proximal levels forms an important intercalating apparatus and, with the nucleus of Perlia which is situated in the more caudal levels, receives innervations from the subcortical and, to a moderate degree, from the cortical regions. He thinks the Edinger-Westphal nuclei regulate all pupillary movements, not because they give origin to radicular sympathetic fibres, but because they receive a great number of fibræ rectæ.

We wish to thank Dr. William G. Spiller for his valuable assistance and suggestions in the preparation of this report.

REFERENCES.

[1] Atland. *Arch. Ophthalmol.*, 1909, **38**, 296.
[2] Beaumont. *Trans. Ophthal. Soc. U. Kingdom*, 1900, **20**, 228.
[3] Brouwer. *Zeitschr. f. d. ges. Neurol. u. Psychiat.*, 1918, **40**, 152.
[4] Collier, J. S. *Brain*, 1927, **50**, 493.
[5] Collins. *Internat. Congr. Ophthalmol.*, Washington, 1922, 103-143.
[6] Donaldson, H. H. "The Growth of the Brain," New York, 1898, 342.
[7] Fuchs. *Arch. f. Ophthalmol.*, 1890, **36**, 234.
[8] Greenfield and Stern. *Brain*, 1927, **50**, 652.
[9] Gruenstein and Georgieff. *Zeitschr. f. d. ges. Neurol. u. Psychiat.*, 1924-25, **94**, 483.
[10] McMullen and Hines. *Brit. Journ. Ophthalmol.*, 1921, **5**, 337.
[11] Oppenheim. "Lehrbuch der Nervenkrankheiten," 7th Edition, 1923, **1**, 333.
[12] Paton, L., and Mann, I. C. *Trans. Ophthal. Soc. U. Kingdom*, 1925, **45**, 610.
[13] Siemerling. *Arch. f. Psychiat.*, 1891-92, **23**, 764.
[14] Spiller, W. G. *Amer. Journ. Med. Sci.*, 1919, **15**, 695.
[15] Wilbrand und Saenger. "Die Neurologie des Auges," 1900, **1**, 117.
[16] Winkler. "Manuel de Neurologie," 1927, Tome i, "L'Anatomie du Système Nerveux," Troisième Partie.
[17] Yuma Sunaga. *Zeitschr. f. d. ges. exp. Med.*, 1927, **54**, 366.

THE CEREBROSPINAL EPIDERMOIDS (CHOLESTEATOMATA).[1]

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AND

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	PAGE
Introduction	334
Historical	335
Pathology—Types of Epidermoids	339
Nomenclature	363
Clinical Aspects, with Personal Cases	365
The Spinal Epidermoids	377
Summary	382

Introduction.

So many excellent papers have appeared lately on the subject of cholesteatomata of the brain that some explanation may be necessary for the appearance of another contribution. The first excuse lies in the relatively large number of cases which we have collected; moreover, we have been able to include a case of spinal cholesteatoma, which stands out as a particular rarity among a very uncommon class of tumours.

The present chaotic state of our knowledge as to the nature of these growths justifies an attempt at sifting the complicated evidence and placing the problems of histogenesis and pathology in a clearer perspective. Many of the contributions to this subject have done little to elucidate the complexities but have tended rather to obscure the issue, by complicating the terminology, by describing tumours of different types under the same name, or by giving different names to the same type of neoplasm. No less than nine distinct varieties of growth have at various times been spoken of as "cholesteatoma."

Roussy and Cornil [47] have indeed insisted on the fact that the term cholesteatoma cannot serve to define one variety of tumour; in their own words it can concern either inflammatory pseudo-tumours, or

[1] Work carried out at the National Hospital, Queen Square, London, under the auspices of the Medical Research Council.

tumours of the most diverse origin and nature which in the process of degeneration become laden with cholesterin.

Again, there has been much discussion in the past as to the histological type which these tumours represent; they are called epithelial by some, endothelial by others, while some authorities are unwilling to express any opinion as to their nature. The exact point of origin has again been in dispute; one school of thought, for example, attributes the neoplasia to an overgrowth of an inclusion of fœtal cells; others look to the various components of the meninges as the source, and believe in an excessive growth of certain cell groups, which may or may not undergo metaplasia.

Lastly, the question of an uniform nomenclature is still a vexed problem. For reasons which will be given later, we shall adopt the term "epidermoid" as synonymous with that type of cerebral cholesteatoma exemplified by our personal cases.

Historical.

The story of the cholesteatomata has been told on many occasions. It is advisable, however, to review once again the chief milestones in the study of these tumours in order fully to appreciate the complexity and difficulties of the present situation. An exhaustive recapitulation of the literature is not necessary and it will suffice to recall in brief the outstanding contributions to the subject.

Verattus [58], 1745, is usually quoted as being the first to record one of these tumours, but the possibility that it was a teratomatous type of growth and not a hair-containing cholesteatoma cannot be overlooked. His patient, a woman aged 40, whose health had hitherto been uneventful, sustained a sudden ictus; on the third day she became febrile; the following day her temperature was higher, and she died on the fifth day of her illness. Autopsy examination revealed a brain tumour containing masses of hair. There were no bulbous roots to the hairs, both ends of which tapered. Verattus remarked upon the occasional occurrence of hair-containing tumours in other parts of the body, but stated that the presence of such growths within the brain must be extremely rare; he was at a loss to explain their origin within the cerebrum, since fatty tissue did not occur here.

Duméril [13], in 1807, exhibited some pathological wax models before the Société de Médecine, including one of a brain tumour. This was white and silvery on the outside with a greyish-white interior and grew in the cerebellum, apparently from the fourth ventricle. No

clinical notes were available, but Cruveilhier, who quoted this case twenty years later, stated that it had occurred in Dupuytren's service at the Hôtel Dieu in the period 1803-1804. Dupuytren himself confessed ignorance when questioned about the case.

Le Prestre [29], 1828, described under the title of *tumeur adipociriforme* a growth lying in the median excavation of the brain, growing backwards to the left, compressing the pons, medulla and cord. The author described the macroscopic appearance in the following words: "Mamelonnée, dont les granulations sont en tout semblables à des perles, l'aspect aussi brillant que l'intérieur de certaines coquilles. Coupée dans son milieu, elle paraît formée de couches concentriques, unies entre elles par des laines de tissu cellulaire. On n'y observe aucune trace de vaisseaux; sa couleur est d'un blanc opaque, sa densité plus considérable que celle du cerveau." Full clinical particulars were given.

In the following year appeared the work of Cruveilhier [11], to whom we owe the earliest complete description of a specimen and the first commentary as to its nature and source of origin. To him also we owe the term "tumeur perlée." In his case, a growth was found at the base of the brain distorting in an upward direction the vault of the third ventricle and the corpus callosum; it filled the median excavation and advanced as far forwards as the pituitary, distending the optic commissure. The exterior of the growth was of a "metallic sheen like silver or like a pearl of the finest water." It was covered by adherent arachnoid and on cross-section it revealed a yellow-white interior of the consistency of soft wax. According to Cruveilhier, the tumour was a product of secretion which had obviously originated in the serous subarachnoid cellular tissue. No histological description was given, but a chemical analysis was made by Bannel with the following result: "The crystalline nacreous material presented all the characters of cholesterin; the concretional material approximated closely in nature to stearin."

In 1834, Peyrot [43] reported the case of a mirror-maker, a sufferer from chronic hydrargyria, who died suddenly at the age of 36 from an hæmoptysis. Post-mortem examination of the brain revealed at the posterior end of the pons a tumour, the size of a small nut—"formée par des paillettes nacrées, et tout à fait semblable à celles déjà décrites dans l'ouvrage de M. Cruveilhier." This neoplasm, which was adherent to the cerebellum, was covered by arachnoid.

Five years later appeared a record of two cases of "geschichtete

perlmutterglänzende Fettgeschwülste" by Müller [38], who first employed the term "cholesteatoma."

Adams, in 1851 [1], gave the first description in this country of one of these tumours, and he also furnished a good histological account. In his case the tumour, which lay beside the pons, was described as having a mammillated surface, smooth, translucent and pearly. Microscopic section revealed a thin membranous layer "like tessellated epithelium." In the interior the cells were extremely pale and delicate, irregular in outline and were mostly without nuclei. Here and there were plates of cholesterin. Adams compares his tumours with those of Müller's.

Three years later appeared von Remak's paper, in which for the first time we find the suggestion that these tumours may have arisen from misplaced epithelial tissue (" . . . die vielleicht schon auf einer frühen embryonischen Entwicklungstrife").

In 1855, Virchow [59] described a number of cases of cholesteatoma, some of them visceral and others intracerebral; in two cases the tumour arose within the substance of the temporal bone. Virchow suggested the term "margaritoma," but adopted in the main Cruveilhier's expression, and spoke of them as "Perlgeschwülste."

The first case of cerebral cholesteatoma, which was operated upon, was described in 1856 by Esmarch. The tumour in this case appears to have grown from the cranial vault in the frontal region. Numerous other examples were then recorded—mostly either in the nature of isolated case reports or else mentioned in discussions upon cerebral tumours in general. Thus, in this country we had the cases recorded by Peacock [41], Wilks [61], Price, Knowles. In France we had the cases of Spillmann and Schmidt, and in later years Parent-Duchateler and Martinet, and Marie and Roussy. Most of the cases, however, were recorded in Germany, as by Ladame, Bernardt, Petrina, Eberth, Mayer [37] and Foerster. To Eppinger [1875][1] belongs the credit of being the first to record an instance of a cholesteatoma growing within the spinal canal.

The literature now becomes more critical and the questions of origin and histological identity come up for discussion. Perls [42], in 1877, was the first to cavil at the accepted conclusions of his time, and he suggested that the cholesteatomata were of endothelial origin. He further specified the endothelium of the neural lymph spaces as the

[1] Eppinger, *Prag. Vierteljahrschrift*, 1875, quoted by C. Frank.

site of origin. In this view he was supported by Frank, Schmaus and Nehrkorn. Beneke, too, supported this view, but altered his opinion later.

In 1897 appeared Bostroem's [9] masterly and meticulous work on the intracranial cholesteatomata, lipomata and dermoids. He reviewed all the cases hitherto recorded, numbering thirty-two in all, and added two others of his own. Full pathological investigations were made, and Bostroem leant strongly to the view of an epithelial origin. He suggested the title "piale epidermoïde," and stated that they arose from embryonic skin elements at a comparatively late stage; he brought them into line with the pial dermoids, which arose from epiblast of an early embryonic type, and later produced both epithelial and connective tissue elements.

A contribution to the problem now came from America, where Blumer [8] (1900) made an excellent summing-up of the situation as it existed at that time. He added a personal case which proved microscopically to be of endothelial type; the epithelial nature of the typical cholesteatoma seemed to him beyond question, so he tentatively postulated the existence of two or more varieties of tumour, the one epithelial, and the other endothelial, his own case belonging to the second group. Blumer furthermore pointed out the similarity in structure between his specimen and the so-called cholesteatomata of the lateral ventricles found in horses.

No important contribution—other than a few isolated case reports—appeared for the next twenty years, until the publication of Bailey's paper [2] in 1920. Bailey rediscussed the problem with admirable clearness, and added two personal cases: from a study of the literature he estimated that sixty-two cases of cholesteatomata had been recorded up to date. He gave a pathological description and considered the tumour as being composed of four concentric layers. Although inclined to favour the theory of epithelial origin, he regarded the exact site of origin as uncertain. For this reason he rejected Bostroem's title of pial epidermoid and reverted to the expression "pearly tumour."

In 1922, Horrax [20] reported three more cases, some of which contained hair. He again brought them into line with dermoid tumours, which he believed differed only in the degree of inclusion of the original dermal layer. Horrax preferred the term "cholestatoma" which he qualified by prefixing "meningeal."

The same year Cushing [12] recorded the case of an "epidermal cholesteatoma" growing within the skull bones, and he collected from the literature some ten other similar cases.

Bailey's second paper [3] appeared in 1924, and in it further cases were added to the literature.

The last noteworthy contribution appeared in 1925, when Kakeshita [23] dealt with the pathology of two specimens belonging to the Neurological Institute of Vienna. This paper is of interest in that the author appears as a modern exponent of the theory of endothelial origin.

Pathology.

The naked-eye appearance of these tumours is in most instances so constant and characteristic as to render possible a correct pathological diagnosis at sight. According to the site of growth and length of history, the size varies, but as a rule the tumours are of some magnitude at the time of operation or at autopsy. Thus, the tumour may attain the size of a large orange, and weigh as much as 70 grm., as in Kay and Pack's [25] case. They are usually ovoid or spheroidal in shape; the surface is not uniform but is irregularly lobulated (*mamelonné*). The most characteristic feature, however, lies in the well-known appearance of the capsule, which is opaque, white and glistening. So striking is this appearance that it never fails to cause comment and has impressed every observer. At various times the capsule has been compared with silver or with the interior of a shell. The commonest term, however, is that of "pearly tumour," an expression originally employed by Cruveilhier and still in use by many.

Although this pearly exterior is so outstanding a feature at operation, the sheen tends to become dull and finally disappears when the tumour has been preserved in formalin. Museum specimens, therefore, seem disappointing when compared with the appearance or descriptions of the tumour *in vivo*. In certain cases (Case 3) this nacreous capsule is surrounded by a fibrous capsule which loosely envelops the tumour. This is by no means constant, however, and was absent from the majority of our cases. Sometimes, in the fresh specimens, glistening crystals of cholesterin may be seen adhering to the surface of the tumour.

The adjacent brain tissues are usually in no way infiltrated by the neoplasm but are sharply demarcated. With tumours of large size some degree of compression is inevitable. In those rare instances in which the tumours appear to grow within the substance of the brain, Benda [4] has shown that there is an actual invasion and destruction of nerve-tissue. A more or less intimate association with the pia-arachnoid and a definite point of attachment is demonstrable in most of the cases.

The cholesteatomata are firm but brittle on palpation, and possess none of the hardness of some of the endotheliomata and fibromata. The capsule is apt to separate from the bulk of the tumour with the slightest roughness of handling and the rest of the neoplasm then tends to fragment. True cystic degeneration is not seen, but in old-standing growths the interior caseates and undergoes necrotic change, giving rise to a sensation of "yielding" to the finger.

The cross-section also presents a characteristic appearance. The cut surface is usually uniform in consistency from without inwards; it is composed of finely granular material, sometimes showing a flaky or laminated tendency. At various times the tumour on cross section has been compared with sago, marzipan or cocoanut icing. Müller used the expression . . . "zerworfener Felsmassen von geschichteter Bildung." In the fresh specimen the colour varies from white to cream or pale yellow: after preservation in formalin the colour becomes less vivid. If the cross-section is made in another plane the growth is seen to be composed of concentric laminæ and the appearance is not unlike that of an onion. The actual surface on cross-section may give a characteristic soapy or waxy feel to the finger, and the greasy nature of the tumour is frequently betrayed by its effect upon the knife. Some writers have drawn attention to a peculiarly fatty and distinctive odour given off by the growth when cut across.

In some of the recorded cases (although not in any of our present series) hairs have been visible. As a rule they are few in number and appear to grow from the capsule and to extend inwards into the main mass of the tumour. At the point of attachment to the pia the hairs tend to be most numerous.

A noteworthy feature of the epidermoids is the rarity or absence of blood-vessels.

It is obvious from a consideration of the recorded cases that there are particular sites of election for the growth of these tumours. Most of the epidermoids arise from the subarachnoid cisterns. Those which are most anterior in their site of origin tend to fill the cisterna interpeduncularis, and by upward extension they may come into close relationship with the third ventricle. In some instances the epidermoid seems to arise from the apex of the invagination of the pia-arachnoid which forms the velum interpositum and pushes forwards the posterior wall of the third ventricle. A very common site is below the tentorium cerebelli. Here they grow in one of two chief situations; they may fill the whole of the lateral recess and become closely associated with the

peripheral course of the fifth, seventh and eighth nerves, or they may appear on the ventral aspect of the cerebellum, lying strictly in the middle line. In the latter case the site of origin is apparently at a point within the fourth ventricle, and a longitudinal section through the vermis reveals the cavity of the ventricle distended and entirely filled with neoplastic tissue. A few cases of epidermoid tumour are encountered in situations remote from those just mentioned. Thus, in a few recorded instances, a tumour has been described lying within the substance of the

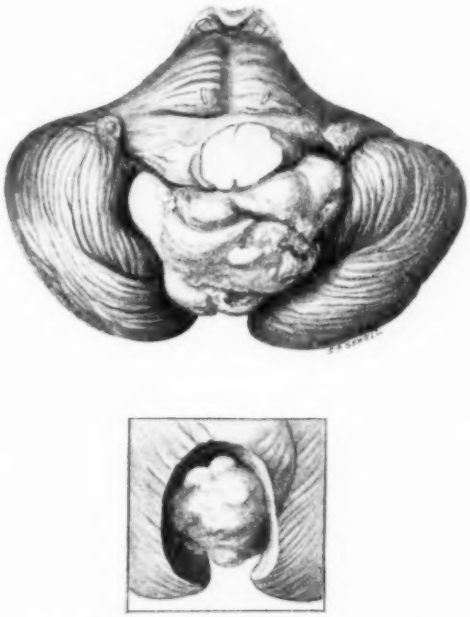

FIG. 1.—Epidermoid of the fourth ventricle (from the Museum of the R.C.S. 1459. 1). The patient, a woman aged 30, was admitted to hospital with a three weeks history of occipital pains, inability to walk, and dysæsthesiæ in the hands. She was dull, tremulous and dysarthric; gait ataxic; knee-jerks exaggerated; defective muscle sense in arms. (See KNOWLES, *Lancet*, 1902, i, 1833.)

hemisphere (cf. Cases 7 and 8). The temporal lobe is then the most usual region; under favourable circumstances it is generally possible to demonstrate a more or less delicate connection between the growth and the leptomeninges of the base.

The histology of these tumours is remarkably constant in appearance and arrangement. Variations do occur, however, between individual

specimens, but only in minor particulars, and the variability mainly concerns the proportionate distribution of one constituent compared with another. In the earlier recorded cases the microscopic descriptions are strikingly uniform, and the nature of the growth is quite clear from the accurate reports.

Cruveilhier did not furnish any histological details in his original paper, although he gave the results of chemical analysis. We owe the first account in this country of the microscopical appearance to Adams; he spoke of a thin membranous layer "like tessellated epithelium"; the cells were described as being extremely pale and delicate and generally without nuclei; they had irregular sides. Plates of cholesterin were visible in the substance of the tumour. Later descriptions emphasized the peculiar structure of the capsule, which we learn was composed of flattened epithelial-like cells, resembling in appearance and in staining properties the cell elements of the skin (Virchow, Benda, Bostroem and others).

Following the precedent of Percival Bailey, one usually considers the epidermoids as being made up of four concentric layers of different thickness, named, from without inwards, the stratum durum, the stratum granulosum, the stratum fibrosum and the stratum cellulosum. Each of these layers is liable to become detached and to lie free. As a result, the epidermoids are difficult to fix and cut satisfactorily, and the microscopic picture is usually fragmentary and ragged.

Most externally lies the stratum durum, which is variable in thickness in different specimens. This is the layer which is responsible for the typical nacreous sheen. In some instances, as in Marie and Roussy's case and our Case 3, it may be so thick as to constitute a tough fibrous envelope. It readily becomes stripped off, so that it is usually seen as a laminated mass lying independently of the stratum granulosum. Layers of collagen fibres, with little or no trace of cellular formation, constitute the minute structure. The individual fibres are loosely packed and when seen longitudinally are wavy in outline. In the deeper parts immediately overlying the stratum granulosum there may be a tendency towards densification. Occasionally in these deeper layers oval cells are seen with their long axes lying horizontally; the nature of these is doubtful, but some of them resemble plasma cells.

Beneath the stratum durum lies the characteristic layer which constitutes the histological criterion of the epidermoids. The stratum granulosum, as it is called, is essentially a cellular layer which stands out in vivid contrast with the rest of the tumour both in appearance

and in staining properties. As a rule there is a narrow interval which separates the stratum durum from the stratum granulosum. The depth of the granular layer varies with the specimen; in some instances (e.g., Case 2) it is only one or two cells in thickness; in others (e.g., Case 9) it may be built up of ten or more layers of cells which vary in character according to their depth. This layer stains intensely blue with iron hæmatoxylin, which is not only taken up by the nucleus and all its granules but also by the cytoplasm itself. The typical cell is a comparatively large, oval or circular structure with a large rounded nucleus. The cells are not packed tightly together, but clear intercellular channels separate one from another. It is occasionally possible,

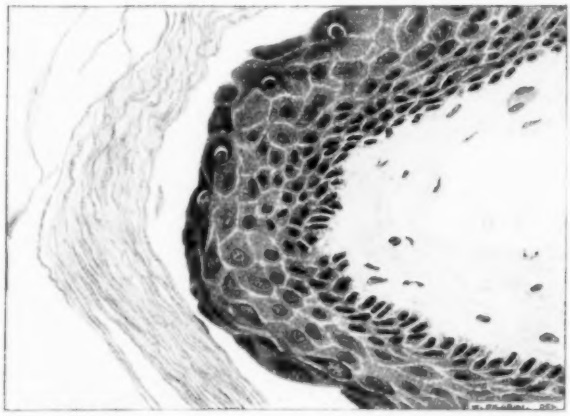

FIG. 2.—Section of tumour from *Case* 9. Here there is a very wide epithelial layer composed of several rows of cells with an arrangement and appearance which alters in the characteristic fashion according to the depth.

as in Case 9, to demonstrate intercellular bridges surmounting these moat-like spaces and connecting adjacent cells. Benda was the first to describe these bridges, and other observers have at times succeeded in demonstrating them; in most specimens, however, they are not visible. Fine granules, composed of keratohyalin, are scattered throughout the cytoplasm. The chemical nature of these granules is identified by their staining reactions with Heidenhain's iron hæmatoxylin, Delafield's alum hæmatoxylin and with Kresyllichtviolett. In the deeper layers of the stratum granulosum the granules become larger and more numerous.

The morphological characters of the component cells vary according to their depth. Immediately below the stratum durum the cells are oval and are arranged tangentially to those in the overlying layer. A palisade formation may therefore result, provided that the section is cut in an accurate transverse direction. Granules are less easily seen here partly because the nucleus stains intensely dark and occupies almost the whole of the cytoplasm. Below this layer is an intermediate zone of rounded cells; the apposition of one cell to another is loosest here and the intercellular channels are clearly seen. There appears to be no definite cell arrangement. In the deepest layers the cells are more oval and are arranged with their long axes parallel with the stratum

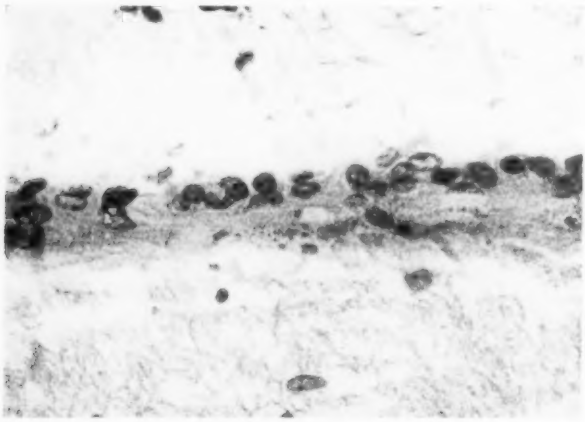

FIG. 3.—Microphotograph of the epithelial layer of *Case* 4, showing granules of keratohyalin (hæmatoxylin and van Gieson preparation).

durum. The nucleus stains less darkly and does not completely fill the cell; granules are here very numerous.

Here and there the stratum granulosum appears to send papillary processes into the more superficial stratum durum; in such places this particular stratum is thicker and may comprise six to ten cell layers.

The majority of tumours, however, possess a comparatively thin stratum granulosum, which shows no evidence of a papillary formation. In such a case the stratum consists of a superficial layer of large swollen cells, polygonal in outline, with pale, oval and faintly staining nuclei, and a granular cytoplasm; between the component cells are definite clear channels. An indeterminate layer occupies the central area and

is made up of a structure in which the outlines of horizontally flattened cells are barely visible. Deepest of all comes a single layer of ill-defined cells bearing numerous pigment granules.

There is usually a sharp line of demarcation between the stratum granulosum and the deeper layers of the tumour; frequently there is an actual gap between the two zones. Bailey speaks of a stratum fibrosum and of a stratum cellulosum as comprising the innermost zones of the neoplasm. These terms are not entirely satisfactory, however; a clear differentiation into two strata has not in our experience been possible; the tissue which immediately underlies the stratum granulosum seems

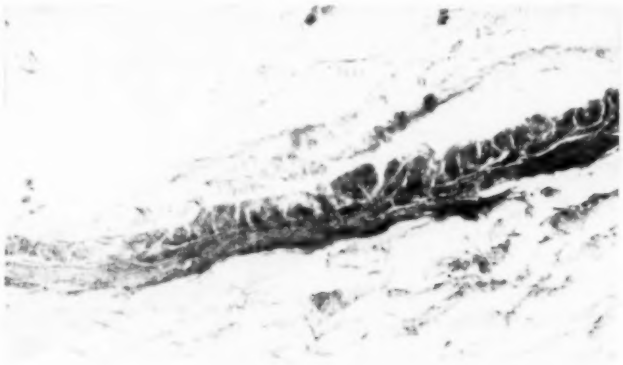

FIG. 4.—Microphotograph through the stratum granulosum of *Case* 7. The appearance is typical of the narrow type of epithelial layer. (Hæmatoxylin and eosin preparation.)

to pass by a gradual transition into the main central mass of the epidermoid. The superficial appearance of the layers deep to the stratum granulosum bears some resemblance to the stratum durum; it is made up of loosely packed layers of wavy homogeneous laminæ with the staining properties of keratohyalin. No stray cells are seen in this zone. The laminæ appear somewhat like fibrous tissue, but differ in their staining properties; they do not stain by van Gieson's method, and in aniline blue-orange-G preparations they are coloured quite differently from fibrous tissue and appear usually as a yellowish structure.

The interior of the neoplasm is made up of similar laminated tissue, arranged in a very loose mesh. In places, the cell outlines are

visible but no nuclei are seen. The fresh specimens show in this area numerous flat cholesterin crystals, but in the process of fixing and dehydration the cholesterin becomes dissolved out. Nehrkorn compared the structure of this zone with the histological appearance of plant tissue; for this reason Bailey proposed the name stratum cellulosum. This term, however, is apt to suggest a cellular type of structure and the original botanical significance may be overlooked. Perhaps a more appropriate name for the tissue constituting the bulk of the tumour would be area cornea, as implying a similarity in appearance and chemical properties with the most superficial elements of the dermis.

Throughout the whole of the tumour blood-vessels are not seen and there is an absence of vascularity.

It is clear from the description of these tumours that we are dealing with an epithelial neoplasm. The essential layer is the so-called stratum granulosum, which is obviously composed of epithelium varying from stratified to cubical in character. Mesoblastic tissues, where present, serve merely as supporting structures. The nature of these tumours can be best understood by regarding them as epidermal in character. The cholesteatoma is made up of an external epithelial membrane, outside which is a delicate fibrous tissue envelope. The interior of the tumour is composed of the accumulated products of the desquamated epithelial layer. In other words the stratum granulosum corresponds with the dermis and the area cornea with the stratum corneum of the skin and a débris of cast-off dead and horny scales.

Examining this premise more closely, the epithelial layer of the cholesteatomata apparently corresponds with several layers of the dermis. Most superficially we have the rete mucosum with its large loosely packed pale prickle-cells and clear intercellular channels; in the most external layer of all the cells are arranged in a fashion recalling a palisade appearance. Most internally is a layer of flattened pigment-laden cells, which is obviously analogous to the stratum granulosum of the skin. The homologue of the stratum lucidum is in places suggested by a narrow layer of indistinct, pale cells lying between the stratum granulosum and Bailey's stratum fibrosum.

In the area cornea we obviously have the retention products of shed horny squames, which are in the most part without nuclei. The presence of cholesterin crystals in this zone is explained by the breakdown of keratin and keratohyalin.

Support is given to this theory of the epithelial and epidermoid

origin of these tumours by the not infrequent finding of hairs within the neoplasm. Originating in the epithelial layer, they usually grow inwards so as to project into the mass of the tumour. The question of the occurrence of other specialized epithelial structures, such as nails and teeth in the cholesteatomata, will be discussed later, when the association of the dermoid and epidermoid tumours is dealt with. The presence of these and other structures of mesoblastic origin will obviously depend upon the depth of the original epithelial anlage.

Despite these striking arguments suggesting that these tumours are of epithelial nature, certain writers, as we have seen, regard them as endothelial. The argument has been reopened in recent years by Kakeshita, who, as we shall see, described the histological details of two cases and regarded them as cholesteo-endotheliomata. The story of this discussion may be briefly outlined.

Von Remak's hypothesis as to the epithelial nature and origin of these tumours remained unchallenged for many years. In 1877, however, in his textbook of pathology, Perls made the unconventional statement that "with reference to the cholesteatomata of the cerebral envelopes, it is very probable that one is dealing with an overgrowth of the endothelium of the perivascular lymph spaces; hence they are pure endotheliomata." He admits the existence, however, of transitional hair-containing forms suggesting an epithelial influence, and brings them into line with the dermoids. Other German lexicographers followed this opinion; Klebs [26], for example (1889), agreed that these growths were endothelial in type. Schmaus (1895) [49] too subscribed to this viewpoint. Glaeser 1890 [16] believed that the cholesteatomata arose from proliferation of the subarachnoid epithelial cells, as a result of some unknown stimulus. At first the growth occurs in scattered islets, but later the connective tissue atrophies and the isolated masses then run together. As the result of pressure the growing cells become flattened so as to form scales. Although it was admitted that epithelium is found in those places which are common sites for the cholesteatomata, Glaeser still thought that they were endothelial. He quoted Virchow's views of the metaplasia of tumours and referred to Koster's work on the growth of epithelial cancer from the endothelium of the lymphatics. The author summarized his views in the statement that these tumours resembled epithelial cancer, but they undoubtedly arose from the middle germ layer (. . . "zweifellos von Abkommlengen des mittleren Keimblattes stammen").

In his earlier publications Beneke [5] also favoured the idea of an

endothelial character of these growths; he thought that the cholesteatoma cells, when subjected to a process of silver impregnation, conformed to the endothelial type by reason of the sharpness and regularity of their outlines. Benda, however, demonstrated equally clear-cut cell outlines in silver preparations of known epithelial growths, arising from the cornea. At a later date Beneke became converted to the epithelial school.

In 1897, Nehrkorn [40] recorded a case of a cholesteatoma occurring in a man aged 44, who had shown little physical disability during life, but had altered mentally so that the diagnosis of general paralysis was made. At the autopsy two mother-of-pearl tumours were found; one, a diffuse, broken mass, lying in the region of the pons and upper medulla, compressing the brain and burying the sixth, seventh, eighth, ninth, and tenth cranial nerves on the left side. The second tumour lay enclosed within the substance of the left temporal and occipital lobes, but was connected with the basal meninges in one place. Nehrkorn was unable to demonstrate either keratohyalin or intercellular bridges, and from the reaction of the tissues to various stains, particularly thionin and silver, he concluded that the tumour was of endothelial nature, "in the form of an endothelial pearl tumour."

Blumer's detailed report of a case of cholesteatoma—which is referred to in more detail later on—is a further contribution to the endothelial conception.

But the possibility at once arises as to whether these authors who subscribed to the endothelial theory were actually describing the same type of tumour. It is conceivable indeed that there may be at least two types of growth, superficially of cholesteatomatous nature, but differing in origin. Such a hypothesis seems to be supported by subsequent work.

Thoma [54], for example, takes up a somewhat similar attitude; while apparently advocating the epithelial origin of the cholesteatoma, he also states that tumours of exactly the same structure are found in the leptomeninges, where they apparently arise from the endothelial cells which line the trabeculæ of the arachnoid.

In the later (1910) edition of his Lehrbuch, Schmaus, who it will be remembered was originally an exponent of the endothelial theory, now takes up the view that there are at least two distinct types of cholesteatoma, one consisting of flattened cells, epithelial in origin, and the other which comes into the category of endotheliomata.

Amongst later writers, Bland-Sutton [7], too, inclines towards the

view of an endothelial origin of the cholesteatoma, and tends to use the terms psammoma, endothelioma and cholesteatoma synonymously.

The hypothesis of the endothelial origin of the cholesteatomata has received a further impetus in recent years by the work of Kakeshita. This author (1925) examined with minute care two museum specimens from the Vienna Neurological Institute. The first was a pearly tumour measuring 5·6 × 3·7 × 4·8 cm. lying within the substance of the right temporal lobe; a very definite connection with the basal meninges was, however, apparent. Histologically, the tumour was composed of cells of an endothelial type, which in places became degenerated and elongated in form and in such places took on the superficial appearances of epithelial cells. These were arranged in two or three layers with an almost palisade-like formation. Most peripherally the cells were cuboidal or polygonal, and contained a distinct nucleus. Towards the interior the cells were larger and the nuclei resembled in many respects those of typical epithelial cells. There were no intercellular bridges and no keratohyalin granules. Lipoid was present in most of the cells. The author insists that the cells contained in the tumour walls were typically those of a dural or arachnoidal endothelioma.

His second case was of a tumour the size of a walnut, lying in the fourth ventricle. The external appearances were those of a typical cholesteatoma, and there was a distinct connection with the meninges. The wall of the tumour consisted of a connective tissue meshwork containing round cells in which lay depositions of some homogeneous material. There were two distinct parts to the tumour, one of which was typically endotheliomatous; the other portion contained horny elements. Kakeshita would not allow of a chance juxtaposition of two different types of tissue, as he could trace every type of transition element from one to the other. He concluded that some at least of the so-called cholesteatomata were endothelial in character, and he thought that such neoplasms probably constituted a class of growth which could be termed cholesteato-endotheliomata.

From a study of the photomicrographs which accompany his paper, we cannot see any structures which resemble in any way the tumours in our present series. Kakeshita's cases—judging both from his description and from his illustrations—appear to be examples of an entirely distinct type of growth.

Despite the view of Klebs, Perls, Nehrkorn, and Kakeshita, we cannot subscribe to any hypothesis as to the nature of these tumours other than the epithelial; from an histological study the impression is gained

of an essentially epithelial type of growth. The layer of flattened cells which bears so close a resemblance to stratified epithelium, the interior formed of the aggregation of desquamated scales and their breakdown products; the positive finding of keratohyalin within the tumours; the occasional presence of hairs, all confirm the conception of an epithelial growth. Nor is there any unequivocal evidence which can be quoted to the contrary. The most obvious probability is, of course, that there is more than one type of tumour described as cholesteatoma, the most usual variety—of which our cases are examples—being clearly epithelial; while the other group, of which Klebs and others have written, are definitely endothelial. Of this latter class, we have had no personal experience.

The presence of an heterologous epithelial type of growth, lying in close apposition to the brain and associated more or less closely with the meninges, obviously requires explanation. Two main possibilities assert themselves: as Martin, Dechaume and Puig [36] have stated, the question is whether the epidermoids arise from fœtal inclusion of epithelial cells, or whether they result from metaplasia of the endothelial cells of the meninges.

Virchow was perhaps the first exponent of the metaplasia school. Basing his argument (fallaciously, as we now know) upon the cell clusters occurring in the cancroid, he attributed the growth of cholesteatomata to a metaplasia of similar clusters (Zellzapfen) lying within the layers of the arachnoid. He stated that these cells may be seen exhibiting all stages of cholesteatoma formation, cornification, desquamation of horny elements and cyst formation.

Eberth, and later Glaeser, also favoured the view of metaplasia of the endothelium and perithelium of the arachnoid spaces. Benda also subscribed to a metaplasia hypothesis, but believed that the primary tissue comprised the cells lining the embryonic medullary tube; he tentatively hazarded the possibility that diverticula from the cerebral ventricles might have constituted the starting point of the cholesteatomata (" . . . und mit dieser zusammenzuhangen scheinen, aber durch ihre regelmassigen kubischen Zellen weniger wucheruden Cholesteatomzapfen als kleinen Divertikeln der Ventrickelwand gleichen.")

If the metaplasia theory were correct one would expect to find transition forms between epithelial and endothelial elements occurring in the same tumour; such has not been our experience. Nor can one readily point to any external factor—mechanical or chemical—respon-

sible for transforming one type of cell into another totally distinct variety. The causes of metaplastic tumour formation elsewhere are usually obvious.

We are inclined to favour the view that these tumours are essentially and primarily epithelial, and that they arise not by a process of metaplasia of normal cell structures, but from the overgrowth of epithelial rudiments. We assume a fœtal inclusion of epidermal cells which, according to the depths of the layer or according to its embryonic antiquity, will produce either an epidermoid or a dermoid type of tumour.

The sites of election of the epidermoids have already been discussed; the problem now presents itself as to the possibility of correlating our clinico-anatomical facts with the conception of an epithelial rudiment.

It is tempting to conceive of an inclusion of epithelial cells occurring at the time of the formation of the fœtal flexures. Thus, if at the pontine flexure a few epidermal elements became cut off from the exterior, they would remain in the region of the lateral recess as a potential anlage. In such a manner one might explain the growth of epidermoids in the regions of the cisterna basalis, the ponto-cerebellar angle and the fourth ventricle. A similar cutting off of cells in the region of the cephalic flexure would account for the more anterior cholesteatomata growing in the region of the third ventricle. This viewpoint coincides with that of Scholtz [50], who dates the origin of cholesteatomata from the time of the closure of the medullary tube or of the mouth flexure (third to fifth week).

In this way an adequate explanation can be offered for the occurrence of the majority of the epidermoids, that is to say, those arising from the basal excavation of the brain. The origin of the intracerebral tumours, the intradiploic and the cholesteatomatous growths within the spinal canal will obviously still require elucidation, There is no evident reason why the same factor of epithelial cell inclusion cannot be cited ; indeed, our eighth case seems to lend weight to this idea. The erosion of the skull bones, obviously from a without-within direction, and the presence of paired and identical tumour formations connected through a narrow foramen, suggest that the scalp tumour was the primary one and had later spread into the cranial cavity.

Benda's theory of an origin from the embryonic medullary tube clearly fails to explain all the data ; it cannot account for the occurrence of epidermoids completely unassociated with the ventricles ; it does not easily explain the occurrence of neoplasms lying outside the strict midline of the brain or cord.

In the light of the work of Harvey and Burr [19] on the development of the meninges, the explanation of the occurrence of epithelial elements in association with the membranes becomes intelligible. These authors showed that the view of His and Kölliker—that the pachymeninx and the leptomeninx have a common origin, a primitive mesenchyme derived from a specific germ layer (the mesoderm), is incorrect. They proved, on the contrary, that certain ectodermal elements, derived in large part from the neural crest, are contributed to the mesenchyme and take part in the formation of the leptomeninx.

. . . . . .

It now becomes necessary to consider some of the other varieties of tumour which have been spoken of by various authors as "cholesteatomata." Within this category will be included certain of the suprapituitary cysts; the teratomata of the brain; the endothelial type of cholesteatomata; the epithelial masses associated with chronic ear disease; the so-called cholesteatoma of the ventricles as met with in the horse, and lastly the pearly tumours of the cranial bones.

"*Cholesteatomatous tumours*" (*of Rathke's pouch*).—Before discussing the nature of the intracranial cholesteatomata, it is necessary at the outset to exclude definitely many of the cholesterin-containing juxta-pituitary cysts. The term cholesteatoma has in the past been loosely and inaccurately applied to certain of the epithelial tumours arising from unobliterated portions of Rathke's pouch. Such tumours readily break down to form cysts in which cholesterin is a prominent constituent. Many of these tumours, which have been confused with the cholesteatomata, are true adamantinomata. In others, e.g., Lockwood's case [30], the exact nature of the tumour—although almost certainly epithelial—is less clear. It cannot be emphasized too strongly that the presence of cholesterin within a cerebral tumour does not indicate that the tumour is a cholesteatoma, and for this reason the nondescript term "cholesteatomatous tumour" (or cyst) is better avoided.

Dermoids and the hair-containing cholesteatomata.—Throughout the literature the relationship between the cholesteatomata proper and the intracranial dermoids has been often discussed. Although in the majority of instances the epidermoid tumours are made up of epithelial tissue which corresponds with the superficial or epidermal layer, nevertheless there are cases on record in which hair has been seen in tumours otherwise quite typical. Thus Bostroem, Horrax and others have

recorded cases in which typical pearly cholesteatomata have contained hair. In some there may also have been sebaceous glandular structures present in the neoplasm associated with the hair follicle. Horrax, in a recent paper on this subject, states that the depth of the epithelial cell layer which constitutes the tumour anlage, determines the structure of the subsequent neoplasm. Where the developmental layer has been purely epidermal, there will result the ordinary pearly cholesteatoma or epidermoid, as in our present cases. But if a deeper or dermal layer is concerned, then the other structures, which characterize a dermoid type of growth, will occur in the tumour. Amongst the latter are included the hair-containing tumours. Horrax would classify them all as cholesteatomata, and further specify them as hair-containing or non-hair-containing. Three cases are cited by the author, the first two of which are dermoids and are outside the strict scope of this paper. In the third case, however, the tumour was typically pearly in appearance; it lay in a characteristic site and presented the ordinary histological picture, except for the finding of hair, glandular tissue and a little bone.

Bostroem dealt at some length with the relationship between dermoid and epidermoid growths. In the latter type he was insistent that all the tissue elements should be of epithelial nature. He regarded the dermoids—which contain mesoblastic structures—as arising from a dermis which differed not in actual depth of layer, but in embryological antiquity. A younger and more primitive cell layer, he suggested, will give rise to both epithelial and mesothelial tissues, and will be characterized by a dermoid rather than an epidermoid type of growth.

It seems obvious from the standpoints of both embryology and histology that there cannot logically be any strict or sharp line of demarcation between the epidermoids and the dermoids. Both are primarily epithelial tumours resulting from cell-inclusions, and the resulting structure will depend upon one of two factors. In the first place, the depth of the primitive layer may be the critical factor—the epidermoids arising when the epidermal tissue alone is concerned and the dermoids when the deeper dermal layer is in question. The hair-containing epidermoids—e.g., Horrax's third case—may represent a transition form. On the other hand the age of the primitive layer may be of more importance than the actual depth. Thus, for example, a dermoid type of tumour may result when the cell inclusion takes place at an early embryonic date, while cell inclusions occurring later in fœtal life tend to subsequent epidermoid growths.

If, however, there is but little histological or embryonic distinction between the dermoids and the epidermoids, there appear to be certain points of differentiation from both clinical and anatomical angles. Thus the age factor is of importance, dermoid tumours causing symptoms at an earlier date than the epidermoids. Secondly, the site of origin is important; the epidermoids tend to originate at or near the midline, from the base of the brain, and frequently in association with the third or fourth ventricles. Dermoid tumours, on the other hand, are not uncommonly situated within the substance of the cerebral hemispheres, and may be multiple. The dermoids more often break down in the centre to form cysts, and they are less often covered by the characteristic nacreous sheen. Lastly, the dermoid variety of growth is more often associated with other congenital anomalies and developmental errors.

The cholesteatomatous endotheliomata.—Under the above title Blumer (1900) described two tumours attached to the choroid plexus of a man aged 59. The clinical history is not important. At autopsy, some degree of ventricular distension was seen. Attached to the left side of the choroid plexus was an ovoid nodular mass measuring 2·2 × 1·5 cm. The cut section was mostly mottled and reddish-grey, but numerous small yellow areas were present. A similar tumour measuring 1·8 × 1·2 × 1 cm. lay in the right lateral ventricle. Numerous gritty particles escaped from the cut surface of the mass, which proved to be cholesterin in composition.

Blumer described two distinct histological parts in the tumours, a cholesterin-free and a cholesterin-containing portion. The former was small and situated peripherally, and constituted the nodules which appeared on the surface. Small round or oval spaces associated with the blood-vessels, and containing one to three cells, formed the characteristic feature. The cells were ovoid with a relatively small nucleus; the protoplasm contained fine refractile granules.

In the cholesterin-containing part of the growth were numerous wedge-shaped empty clefts which presumably held cholesterin in the fresh state. Red blood-cells, a few leucocytes and occasional tumour cells, occupied the intervals between the spaces. Changes in the connective tissue gave rise to multinucleated cells, the shape of which depended upon the accommodation between the clefts. In the older portions of the tumour the cholesterin cavities had become narrowed by contraction of newly-formed connective tissue.

Blumer regards his neoplasm as commencing by a proliferation of the endothelial cells of the perivascular lymph spaces, followed by a

gradual thinning of the walls with subsequent escape of blood into them. Cholesterin crystals then appear in the blood-infiltrated tissue; finally, a proliferative process takes place in the connective tissue.

It is obvious from the minute description that this tumour differs markedly from the epidermal tumours forming the subject of this present paper. As Blumer points out, there is an obvious resemblance to the equine psammomatous tumours, and the two growths are probably identical. The author arrives at the important conclusion that there probably does exist a class of cholesterin-containing tumours of the choroid plexus in the human which he proposes to call cholesteatomatous endotheliomata.

Does Blumer's case constitute the solitary example on record of such a tumour? Or is it possible that the cholesteatomatous neoplasms seen by Klebs, Perls, Nehrkorn, Frank [15] and Schmaus and others, who have supported an endothelial origin, were actually tumours of the Blumer variety?

The middle-ear cholesteatomata (cholesteatosis).—By far the largest class of new growths spoken of as cholesteatomata is found in association with diseases of the middle ear; otologists have for many years been familiar with the occurrence of tumour-like masses of epithelial débris, occurring either in the cavity of the middle ear or in its immediate vicinity. There is less certainty as to the exact mode of origin of these formations, and as to the relative importance of various ætiological processes in their causation.

A chronic inflammatory otitis media is almost always associated, and a perforation of the tympanum is practically constant. The aperture is usually present in the postero-superior quadrant of the drum, or else in the membrana flaccida of Shrapnell; cholesteatomata are rarely associated with perforations through the lower half of the tympanum.

There are two main types of cholesteatoma described in this connection; first, there may be an irregular, caseous mass without any definite capsule, composed of epithelial cells, "squames," fat, blood-cells, granulation tissue, bacteria and cholesterin-crystals. Secondly, the tumour may be compact and lamellated, and possess a definite capsule with a brilliant mother-of-pearl sheen. It is probable that this second variety is merely a later stage of the first. The cholesteatomata frequently become infected, and break down in the centre to form a pultaceous and foul-smelling débris.

Both varieties of neoplasm are usually encountered within the antro-tympanic cavity. As the tumour increases in size, it compresses and

finally erodes the surrounding bone and may thus invade the mastoid antrum; sometimes the posterior wall of the cavity is destroyed and the tumour invades the cranial cavity. Here it may grow apace and extending backwards push aside the dura and sigmoid sinus, and distort the occipital and even the cerebellar lobes.

Many speculations have arisen to explain the origin of the aural cholesteatomata. Von Tröltsch (1868) regarded them as retention tumours; Wendt (1873) thought them to be products of desquamatory inflammation of the mucous membrane of the middle ear. The main difficulty has been to explain how a tumour composed of stratified and horny epithelial cell elements could arise in a cavity lined by columnar epithelium. Two main views are held to explain this phenomenon :—

(1) Habermann (1881), Bezold (1889), and others, believe that the tumours arise from a backward growth of meatal epithelium through the tympanic perforation into the antro-tympanic cavity, where, possibly under the influence of toxin stimulation, the epithelium takes on the habit of abnormal growth. Other contributory factors probably are inadequate drainage, whereby the products of excessive desquamation cannot be removed sufficiently quickly.

(2) Many objections have been raised against this view. It has been pointed out that mere epidermal invasion of the middle ear is not sufficient to cause cholesteatomatous growth, for Schwartze (1878) had described epidermic blind pouches jutting into the middle ear and persisting throughout life without tumour formation. Again, there are cases—rare it is true—in which no perforation of the drum is demonstrable through which epidermal invasion can take place. Consequently the theory of metaplasia of the antro-tympanic mucous membrane arose; it is supposed that under the influence of some added factor the columnar epithelium lining the middle ear alters in character and takes on abnormal habits of growth. This point of view has been lucidly expounded by Wingrave [62] (1910), who suggested that this metaplasia is brought about by the prolonged admittance of air into the antro-tympanic cavity, which by lowering the aqueous tension causes desiccation of the mucous membranes. In time this drying process, supplemented by the irritation of bacterial and cytolytic toxins, brings about a true transformation of the mucous membrane. Wingrave compares this mechanism with the well-known phenomenon whereby rectal and nasal polyps which, when they protrude permanently from the orifices, undergo a transformation of their surface columnar epithelium

into a stratified or horny type. The same additional factor of inadequate removal of desquamation products of course plays an important part.

Kutvirt's [27] views as to the origin of the cholesteatomata of the ear are interesting. He attributes the primary change to the necrosis of the bone with cavity formation; the mucous membrane lining the original cavity becomes transformed into stratified epithelium. Accumulation of the desquamated scales leads to the formation of the cholesteatoma.

In recent years, however, Nager, of Zurich, has swung the pendulum of otological opinion back to the view of meatal epidermal ingrowth, for by a beautiful histological preparation he was able to demonstrate beyond any doubt this migration of epithelium through a perforation into the cavity of the middle ear.

A third and very rare type of cholesteatoma is known to the otologists; this variety, originating within the air cells of the mastoid, seems to grow without the additional factors of sepsis and tympanic perforation being required. Thus Lucae (1886) recorded a cholesteatoma arising in the mucous membrane of the tympanic cavity: there was no perforation of the drum and the patient had never suffered from ear disease. Two similar cases were reported by Erdheim. Kuhn reported the case of a man aged 51, who for a year had suffered from tinnitus, deafness and vertigo; the patient then developed a cold which led to a suppurative otitis media and later to a mastoid abscess. Exploration of the mastoid cells revealed a cholesteatomatous tumour, the size of a hen's egg, pressing against the cerebellum and sigmoid sinus. Korner removed a cholesteatoma twice as big as a hen's egg from the interior of the petrous bone. Other cases of so-called "congenital" cholesteatoma (or "cholesteatomum verum") have been recorded by Mondscheim (1911), Hennebert (1912), Maasse (1912), Arbantschitsch (1912), Moller (1918), Shefferd [52] (1922), and Karlefors [24], (1925).

Kirchner (1881) demonstrated by sectioning the bony walls surrounding the ordinary type of middle-ear cholesteatoma that the tumour mass insinuates itself through the interstices of the Haversian canals. It is conceivable that those cholesteatomata which appear to arise primarily within the pneumatic cavities are in reality extensions of the stratified epithelial ingrowth from the middle ear. The more usual view, however, is to regard these air-cell cholesteatomata as primary tumours originating from cell-rests. Presumably then, epithelial rudiments are present in the mucous membrane lining these cavities.

At a later stage we shall discuss the occurrence of cholesteatomata within the diploë of the skull bones at a point far removed from the ear. In such cases there seems to be no question of an origin from intra-osseous cavities lined by mucous membrane. The possibility of the petrous and mastoid cholesteatomata being examples of the larger class of diploic cholesteatomata, although rarely discussed by otologists, requires investigation.

The histological structure of the aural cholesteatomata (both "primary" and inflammatory) bears a close resemblance to the meningeal varieties. The nacreous outer layer is made up of a thickened fibro-vascular stratum in which a few plasma-cells may be visible. Lining this is a layer of stratified epithelium resembling the Malpighian layer of the epidermis. The cells are successively columnar, spheroidal and polygonal from below upwards. Eleidin granules, prickle-cells and papilla formation still further enhance the resemblance to the skin. The bulk of the tumour—corresponding with the horny layer of the epidermis—is made up of closely packed and laminated "squames"; the nuclei are either absent or else only faintly visible. Between the cells lie granules of fat and cholesteatomatous crystals (Wingrave).

Although the clear description given by Wingrave recalls in almost every particular the histology of the pial epidermoids, Bailey believes that the two types of growth can be distinguished and—in spite of the descriptions given—states that there is no epithelial sac and no innermost area of plant-like cells in the aural cholesteatomata. Humiston, too, states that the true neoplastic formation is distinguishable by the presence of a newly formed cyst cavity and wall. We were unable to demonstrate any epithelial cell-layer in the sections of an aural cholesteatoma kindly given us by Mr. Hugh Cairns; the specimens consisted mainly of concentric laminæ which closely resembled the area cornea of the epidermoid tumours.

In view of the important rôle played by chronic sepsis in the formation of the aural cholesteatomata, some distinctive term seems necessary. The nature of the tumour is comparable with the granulomata, in lying midway between the purely inflammatory swellings and the true neoplasia. Humiston and Piette [21] described the middle-ear tumours under the appellation "cholesteatosis," a term which we consider both distinctive and adequate.

Cholesteatoma vasculosa in the horse.—Veterinary medicine has long been familiar with the occurrence of intracranial tumours, which are largely composed of cholesterin and have been termed

cholesteatomata. Gamgee (1859) was perhaps the first to describe such neoplasms, and since that date many other cases have been recorded. According to Dextis, indeed, such tumours were found in 22·5 per cent. of 204 cases examined.

The horse is the animal usually afflicted. The tumour is almost always bilateral and appears to arise from the choroid plexus, to which it is attached by a very fine pedicle. Most of the growth floats loosely in the lateral ventricles, being merely tethered to the choroid plexus. In many instances there are no clinical symptoms, though in some cases the horse has been regarded during life as somewhat stupid and confused; in other cases "staggers" have been noted; rarely does any actual paralysis result.

McCarthy [31] (1904) stated that cholesterin depositions were comparatively frequent in the choroid plexus of animals although rare in man, and he suggested that this deposition process was analogous to calcification in the human subject. Corpora amylacea—common in the choroid plexus of man—are rare in animals.

It is obvious that the histological structure of the equine cholesteatoma is entirely different from the ordinary pial epidermoid in man. The tumour is excessively vascular, contains melanin pigment and is made up of endothelial cells.

Schmey has associated the horse tumours with the xanthomata, and regards them as "Granulationsgeschwülste." Joest confirms this view, and explains the formation in this way: first, the choroid plexus becomes infiltrated with macrophages; crystalline deposits of cholesterin then follow, and set up a connective tissue reaction in their immediate vicinity.

Although the term cholesteatoma has been extensively used in the past by veterinarians, and is in fact still in common use in France, M'Fadyean [32], in 1902, pointed out that this term was misleading. He emphasized the dissimilarity in character between these ventricular tumours and the human cholesteatomata, and proposed that the former should be termed psammomata, although he suggested that they were not identical in structure with the human neoplasms of that name.

The histological structure of an equine cholesteatoma, which was kindly given to us by Professor Hare of the Royal Veterinary College, is illustrated in fig. 5. The bulk of the neoplasm was made up of new-formed connective tissue containing numerous cholesterin clefts. Blood-vessels were abundant throughout the section. In no part of the specimen at our disposal could we find any trace of endothelial cell elements or of epithelial tissue.

Are we justified in assuming that these horse tumours all belong to this psammoma group? M'Fadyean's work in this connection suggests that we are not. In 1902 he reported a case of intracranial growth occurring in the horse and approximating in histological structure to the true meningeal cholesteatoma of man. A second similar case was recorded by himself in 1911 [33]. In his first paper he described the brain of a horse which during life showed some evidences of stupidity. Lying within the posterior part of the left cerebral hemisphere was a cyst the size of a pullet's egg. A thin but tough fibrous envelope surrounded the cyst, which was lined by peculiar glistening superimposed

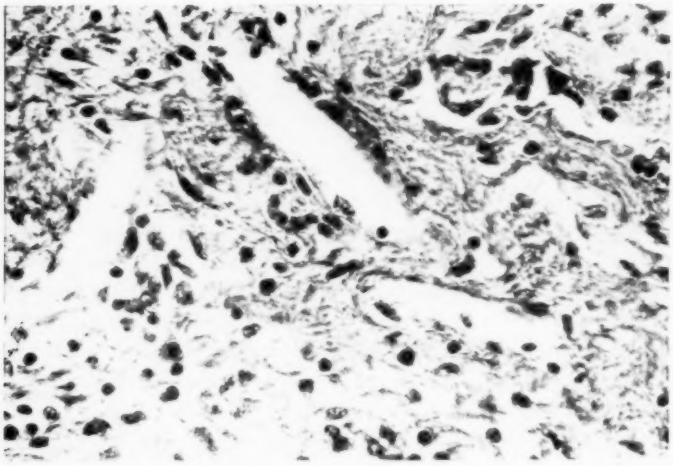

FIG. 5.—Section of a so-called "cholesteatoma of the lateral ventricle" from a horse. Empty cholesterin clefts are surrounded by a cellular connective tissue. No epithelial elements occur.

laminæ—resembling fish-scales. This lining membrane proved to contain no cholesterin. Histological examination revealed an external vascular connective tissue layer bearing many pigment-laden cells within its meshes. The inner layer was epithelial in nature, being composed of several strata; the deepest strata contained cubical or short columnar cells recalling the deepest cell stratum in the skin or mucous membranes. Transitional cells occupied the next two or three layers and led to the layer of cornified cells converted into thin scales without any trace of nuclei, corresponding with the stratum corneum of the skin. It was obvious that the laminated horny mass lying free within the cyst cavity was the product of exfoliation of this horny layer.

M'Fadyean's second case was of a mare which showed some unusual behaviour at the age of 11 years. It improved after two months, but then relapsed into a state of dullness which persisted up to death, one year later. At the autopsy a cystic tumour was found lying in the right cerebello-pontine angle. Blood had extravasated between the tumour and the cerebral hemisphere, and there had been some hæmorrhage into the growth itself. The contents were brown, putty-like and somewhat greasy to the touch. Microscopical examination of the cyst wall revealed a connective tissue membrane surrounding a typical epithelial layer. No hair follicles or glands were present. His paper is illustrated with very good photomicrographs, which confirm the similarity in structure between this case and the human epidermoids. Through the kindness of Professor Hare we were enabled to examine the actual specimen at the Royal Veterinary College.

M'Fadyean's two cases constitute, as far as we have been able to trace, the only instances of true epidermoid tumours in the horse. It is possible that the tumours were of dermoid character, particularly the first case, which we are told grew within the substance of the cerebrum, but the histological description contained no mention of any mesoblastic elements.

The diploic cholesteatomata.—Tumours of cholesteatomatous nature growing within the diploë of the skull bones constitute a small and uncommon group. One of the original cases recorded by Müller [1838] was of a cholesteatoma originating between the tables of the temporal bone. At least ten other cases of this nature have since been described.

The neoplasm apparently originates in the diploë, and in its growth expands both the outer and inner tables. A characteristic pearly appearance is obvious when the thinned, overlying bone is removed. Histological reports, though lacking in detail, apparently indicate that the characteristic epidermal elements are present and that the tumours are of typical cholesteatomatous nature.

There are many clinical points which characterize these diploic tumours. In the first place, trauma seems to play an important active rôle. In at least four of the cases (see table) there was a history of a blow on the head of some severity. Shortly afterwards a swelling appeared below the site of the trauma and increased in size. The lump was tender and at times soft in the centre, with a sharp-edged circumference. Skiagraphy revealed a characteristic change in the cranium. Little or no disability may result from this tumour, at least until many

years have passed; and even when the patient seeks advice the signs of focal disease and generalized increased pressure are only slight. Lastly, a feature of the diploic cholesteatomata lies in their amenability to surgical procedures. In at least eight of the cases the tumour has been removed in toto, without a fatality—a result which contrasts strongly with the usual variety of cholesteatoma. Esmarch's case—the first cholesteatoma to be treated surgically—was of a diploic tumour. We have met with no instance of a diploic tumour in our series.

Reference has already been made, when dealing with the aural cholesteatomata, to the occurrence of primary tumours within the pneumatic cavities without the apparent intervention of sepsis as an ætiological factor. It was suggested that these primary neoplasms may be examples of the diploic cholesteatomata originating in the bones around the ear. If this view is correct, then, to the cases recorded by Müller, Virchow, and Pfannenmüller (in which the cholesteatomata lay in the diploë of the temporal bones) must be added those described by many otologists, particulary Lucae, Erdheim, Kuhn, and Shefferd.

THE DIPLOIC CHOLESTEATOMATA.

Author	Reference	Sex and age	Localization	Duration	Symptoms	History of trauma
Müller	Ueber die feineren Bau, &c., 1838		Temporal	—	—	—
Esmarch ..	A. f. p. A. 1856.20.307	M. 24	L. frontal	14 yrs.	—	—
Weinlechner	W. k. W. 1889.7.136	M. 45	Frontal	37 yrs.	Epilepsy swelling	Blow on head at age of 8
Wotruba ..	W. k. W. 1889.7.889	M. 22	R. frontal	—	Deformity of R. eye	—
Pfannenmüller. .	1895	—	Temporal	—	—	—
Koener	Z. f. Ohr. 1900.37.352	M. 41	L. occipital	Many years	Headache Swelling	—
Blecher ..	D. Z. f. Ch. 1903.70.352	M. 24	L. parietal	10 yrs. +	Headache Swelling	Blow on head as a child
Borchardt ..	A. f. kl. Ch. 1905.77.892	—	—	—	Headache + cerebellar signs	Scalp wound
Cushing ..	S. G. O. 1923.34.557	M. 40	L. temporo-parietal	4 yrs. +	Headache sl. R. hemiparesis	(1) G.S.W. head 10 yrs. (2) Concussion 4 yrs.

Nomenclature.

Not the least of the problems arising during a study of this class of tumour has been the question of nomenclature. At present there is a tendency for the terms "cholesteatoma," "pearly tumour," and even "endothelioma" and "psammoma," to be used synonymously; and furthermore there is a general lack of precision as to the exact meaning of each expression.

The first title, namely, "tumeur adipociriforme," we owe to Le Prestre, but it never gained acceptance.

One of the most generally used terms is that of "pearly tumour." As we have seen, Cruveilhier was the first to use this expression, and in his original paper he laid some emphasis upon the external appearance of these growths. Virchow, writing some five and twenty years later, followed Cruveilhier and spoke of these tumours as "Perlgeschwülste." This title, however, did not gain much popularity at that time, although Rindfleisch, in 1886, employed the modified expression "Perlkrebs." Nehrkorn was almost the only German writer to follow Virchow in speaking of these tumours as Perlgeschwülste. In recent times, Percival Bailey has revived Cruveilhier's original title, and everywhere refers to the "pearly tumours." Bailey gives several good reasons for this: "pearly tumour," he argues, describes accurately the most obvious external characteristic; it describes a feature which is constant; and, lastly, it is non-committal and does not involve any theoretical and unproved consideration of histogenesis, or of site of origin.

Certain arguments may be raised against this nomenclature, however; in the first place, the term "pearly tumour" is purely descriptive, and refers merely to the presence of a glistening nacreous capsule, which in an occasional case may be poorly developed or inconspicuous; secondly, in museum specimens the sheen tends to wear off after immersion in formalin, and in cross-section specimens the pearly capsule may be difficult to find. But more tangible argument is justified when we consider that other discrete though allied growths may have an identical capsule; thus the dermoid tumours, the encapsulated aural cholesteatomata and some of the cholesteatomatous endotheliomata may have similar external appearance, and yet these tumours are separate both in histology and in origin. Finally, Bailey's last argument is a double-edged one; a term which is avowedly non-committal is for that very reason unscientific and undesirable. No hint is given by the term as to

the histological structure of the tumour—a question which to-day seems capable of solution.

The second widely accepted term is cholesteatoma. This is probably the most popular title in modern use. Objections against its employment are clearly manifold, and in fact there is but little to recommend it. All writers agree that cholesterin plays no essential rôle in the histology of these growths, while cholesterin may be present in abundance in many other varieties of intracranial tumour. Secondly, we have seen that there are at least seven different types of growths which are still spoken of as "cholesteatomata." And lastly, this appellation is again a purely descriptive one and gives no inkling as to their histology or origin. Horrax, it is true, has partly amended this defect by prefixing the adjective "meningeal," but the result still falls short of the ideal.

Bostroem made the most serious attempt at a scientific nomenclature with the expression "pial epidermoid." This title did not receive the recognition it deserved however, and to-day it is but little employed. Bailey's chief objection was to the implication it carries: that these tumours are epithelial in structure, and secondly that they arise from the pia. Both assumptions are, according to Bailey, not yet beyond question.

Of the epithelial origin of the usual type of cholesteatomata, of which the nine present cases are examples, we think there is but little doubt. For this reason there can be no objection against the word epidermoid. A pial origin, however, we agree is not only doubtful but even improbable. We would suggest therefore that these tumours be spoken of as "epidermoids" quite simply: such a term is terse, accurate, and conveys the idea of their epithelial nature. The word can be used in ready contrast with the dermoids, which are tumours of analogous origin, but contain elements other than mere epidermal structure.

Confusion need not necessarily arise between the epidermoids and those epithelial tumours arising in association with the fœtal craniopharyngeal duct. We already know sufficient of the latter class to be able to separate off a distinct subtype—the adamantinomata—which probably constitutes the majority. For the remaining types, we may meanwhile employ some non-committal term such as "infundibular tumours," or "epithelial growths of Rathke's pouch," until a scientific and accurate classification is forthcoming.

The Clinical Aspect of Epidermoids.

In Tooth's series of 258 cerebral tumours, there was one cholesteatoma, and in Bernhardt's series of 487 cases there was only one. Out of 550 tumours recorded by Bailey, and 750 recorded by Horrax, there were two cholesteatomata in the former series and seven in the latter. Schulgin [51] (quoted by Meyer) gave the incidence of epidermoids as 0·04 per cent. of all cerebral tumours.

Less than 100 cases of intracranial cholesteatomata have been recorded in the literature; we consider, therefore, that this type of tumour is sufficiently rare to warrant the publication of eight other cases. In addition, a cholesteatoma occurring in the spinal canal is reported later in this communication.

Two or more tumours of this nature have been found on a few occasions, either in the brain or in the spinal cord; in other cases, again, tumours were found both in the brain and in the spinal cord. Carl Frank [14], in 1890, quoted cases recorded by Ladame, Eberth and Eppinger. In Ladame's case there were three tumours—two in one lateral ventricle, attached to the corpus callosum, and one nearby. Several tumours—the size of seeds—were found by Eberth in the region of both Sylvian lobes. Reference will be made, in the section on Spinal Cholesteatomata, to the multiple brain and spinal cord tumours, recorded by Eppinger, Trachtenburg [56], and Raymond, L'Alquier and Courtellemont [46].

Below we give, in detail, the histories, clinical findings and results of eight intracranial cholesteatomata.

Case 1.—Epidermoid of the left ponto-cerebellar angle.

H. G. M., male, aged 27, was admitted to the National Hospital, under the care of Dr. Risien Russell on October 29, 1920. He was well until May, 1920, when he noticed an unsteadiness in his gait. About three weeks prior to admission he suddenly became deaf in the left ear; a week later headache and vomiting commenced. He also complained of a vague difficulty in swallowing and of a mistiness of vision of three months' duration.

The family history was good and, apart from trench fever, he had no previous illnesses. While in the Army in 1916, he was frequently being corrected for holding his head to the left.

On examination he proved himself to be an intelligent man, whose cerebration and co-operation were excellent. He had papillœdema of both discs, with nystagmus, coarse to the left and fine to the right. There was slight dulling to pin-prick over the left side of the face and the left masseter muscle did not contract so well as the right. A watch could be heard at 4 ft. on the right

side but only 1 in. on the left. Further investigation demonstrated that the deafness was due to a lesion of the auditory nerve.

No abnormality was detected in the motor and sensory systems of the arms, legs or trunk. All the tendon reflexes were brisk and equal; the abdominal reflexes were absent and the plantar responses were extensor. The Wassermann reaction in the blood was negative.

A diagnosis of tumour of the left ponto-cerebellar angle was made and Sir Percy Sargent operated on January 28, 1921. A pearly tumour was seen in the left lateral recess, lying beyond the eighth nerve and with the thinned and flattened fifth nerve spread over it; a portion of the tumour was removed. The operation note says that everything was satisfactory. Unfortunately, the patient died later the same day as a result of primary hæmorrhage.

On post-mortem examination the pearly tumour, of which the postero-superior portion had been removed, appeared to be growing inwards into the internal auditory meatus. It covered the left and ventral aspects of the pons and its right border protruded from under the basilar artery. The appearance and site of the tumour are well shown in figs. 6 and 7. The histological appearance was that of a true epidermoid.

Case 2.—Epidermoid of the right ponto-cerebellar angle.

T. O'M., male, aged 28, was admitted to the National Hospital, under the care of Dr. Gordon Holmes, on November 9, 1922. He had enjoyed very good health until 1915 when he was "blown up and buried" by a shell. While at the base hospital he suffered with severe headaches, which were followed a few months later by vomiting. These two symptoms have continued on and off since that date, but they have been much worse since February, 1922. In 1919 he began to stagger to the right; one year later he noted deafness in the right ear. In 1917 he had received treatment for paralysis of the right side of the face.

He was a well-nourished man, with a tired, drowsy manner and slow, unmodulated speech. He had complete anosmia on the right side. The visual acuity in the right eye was $\frac{6}{12}$ and in the left $\frac{6}{9}$; the fields were constricted peripherally, and there were six dioptres swelling of both discs. Nystagmus was present, with slow, coarse jerking to the right and a fine rapid movement to the left. He had a definite weakness of the muscles supplied by the right fifth nerve, together with a sluggish right corneal reflex and hypalgesia of the right side of the face. There was weakness of the right facial musculature and complete deafness in the right ear.

The right arm and leg were weak, hypotonic and inco-ordinate in their movements. His gait was ataxic with a tendency to fall to the right. The diagnosis of a right cerebello-pontine tumour was made. On November 17, 1922, Sir Percy Sargent exposed a tumour of glistening "mother-of-pearl" appearance in the neighbourhood of the posterior aspect of the petrous portion of the temporal bone. The greater part of the tumour was removed with a spoon and suction apparatus.

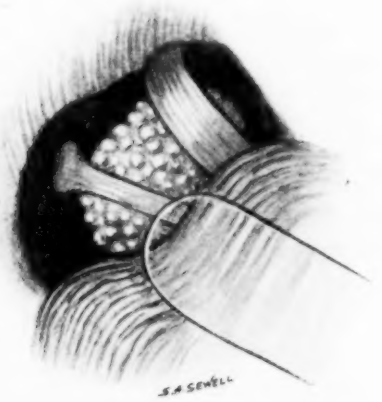

FIG. 6.—Diagrammatic representation of the operative exposure of the tumour in *Case* 1. The flattened fifth and eighth cranial nerves are stretched tightly over the neoplasm. (Drawn from a sketch made by Sir Percy Sargent.)

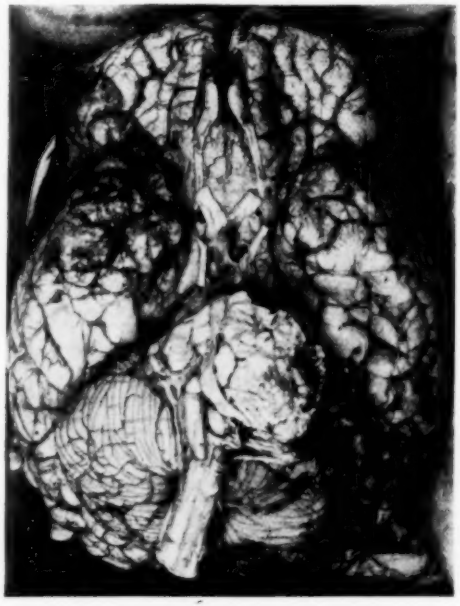

FIG. 7.—Base of brain of *Case* 1, showing a large epidermoid tumour mass occupying the left lateral recess.

The patient died nine hours later from hæmorrhage. On post-mortem examination a typical pearly tumour—the size of a large walnut—lay in the right lateral recess. There was marked indentation and distortion of the right cerebellar hemisphere, and of the right side of the pons and medulla. The fifth, seventh and eighth nerves were stretched and flattened by the tumour, which extended as far forwards as the bifurcation of the basilar artery. Some degree of internal hydrocephalus was present.

The typical appearances of a true epidermoid were seen on microscopical examination.

Case 3.—Mid-cerebellar epidermoid.

C. A., male, aged 37, was admitted to the National Hospital on January 8, 1926, under the care of Dr. Riddoch. He complained of headache, defective vision and unsteadiness of gait of two years' duration. In January, 1924, he began to suffer from attacks of pain in the right occipital region. At the same time the gait became unsteady and the vision in the right eye was misty. After six months' treatment in hospital, he was able to resume his work and remained well until July, 1925, when the headaches and unsteadiness again appeared.

There was nothing of importance in the family history, and he had no previous illnesses.

On examination, he was a well-nourished man of normal intelligence. The visual acuity was $\frac{3}{60}$ in the right eye and $\frac{6}{12}$ in the left. Both discs showed papillœdema and in addition the right disc was covered by a "veil" of connective tissue. The right field of vision was constricted peripherally and contained a large, central scotoma; the left field was normal. Nystagmus was present, coarse on looking to the right, finer and more rapid to the left.

The arms and legs were slightly ataxic, otherwise there was no abnormality of the limbs. The Wassermann reaction in the blood was negative. On February 12, 1926, Sir Percy Sargent removed a large portion of the occipital bone and the arch of the atlas. On opening the dura mater, a glistening mass, which filled the cisterna magna, was seen beneath the arachnoid. The membranes were dissected off and a typical nodular, glistening "pearly tumour" was exposed. A portion of the tumour was removed, but it was impossible to remove the part which was herniated through the foramen magnum.

The temperature rose to 102° on the third day after operation and remained elevated, ranging from 100° to 105° F. until death. He complained of severe headache, backache and neck stiffness; his condition gradually deteriorated, until death occurred on April 15, sixty-three days after operation. The cerebrospinal fluid was examined on six occasions. On February 21, it was a yellow fluid with a fine coagulum and deposit, which consisted chiefly of polymorphonuclear cells. The total number of cells, apart from the coagulum, was 820 per cubic millimetre. On chemical examination, the total protein was 0·18 per cent., glucose 0·022 per cent., chlorides 0·685 per cent. The cultures were negative.

The post-mortem note says: "On removing the skin flap, a quantity of sero-purulent material escaped from an aperture in the newly-formed membrane. Stained films of this exudate showed numerous organisms. On removing the brain, there was no evidence of meningitis. The cholesteatoma, which appeared to be still growing, was situated in the midline between the cerebellar hemispheres."

A sagittal section of the brain is shown in fig. 8. Histologically, this tumour was a true epidermoid.

FIG. 8.—Sagittal section of brain of *Case* 3. The tumour occupies the region of the fourth ventricle.

Case 4.—Epidermoid, posterior end of corpus callosum.

J. S., male, aged 28, was admitted to the National Hospital, on May 20, 1927, under the care of Dr. Grainger Stewart. He complained of headache, dizziness and double vision of three months' duration, although he had not been well since he was taken prisoner of war in 1918. He had appendicitis in 1918, an operation for fistula-in-ano in 1920, and six minor operations on his jaw in 1925.

On examination, he was a well-nourished man of normal mentality. The visual acuity was $\frac{6}{6}$ in each eye, but the visual fields were constricted peripherally, and both fundi showed hæmorrhages and swelling of the discs. The pupils reacted very sluggishly to light, but well on accommodation. There was a bilateral external rectus paresis with well-marked proptosis, but the vertical movements were full.

The muscular and sensory systems were normal, and there was no constant

localizing feature in spite of repeated examination of the reflexes. The Wassermann reaction was negative in the blood and the cerebro-spinal fluid was normal. Examination of the blood and renal efficiency revealed no abnormality.

The diagnosis was doubtful, but in view of the diminution in the visual acuity Mr. Armour made a right fronto-parietal decompression on July 31, 1927. The skull was abnormally thin and the dura mater was very tense. The convolutions over the right frontal lobe were broad and flattened but no tumour was seen or palpated. The patient died later the same day.

On cutting the brain in the sagittal plane, a large round pearly mass was seen extending from above the pineal body to the inferior surface of the splenium of the corpus callosum. It had pushed the posterior wall of the third ventricle forwards and passed as far anteriorly as the foramen of Munro. It

FIG. 9.—Sagittal section of brain of *Case* 4. The tumour distends the third ventricle, which is dislocated upwards and actually lies as an invagination into the lateral ventricle.

measured 4 cm. from side to side, and appeared to arise from an invagination of the meninges between the corpus callosum and the pineal body. Fig. 9 shows the appearance of the brain in sagittal section. The microscopical appearance of the stratum granulosum is seen in fig. 3; the sections showed the characteristics of a true epidermoid.

Case 5.—Epidermoid, right extra-cerebellar region.

M. D., male, aged 41, was admitted to the National Hospital on June 6, 1910, under the care of Dr. Batten. He complained of headache, giddiness, attacks of vomiting and fits, of nineteen months' duration. The family and previous histories were good.

On examination, he was a well developed man of normal intelligence; his speech was normal. The visual acuity was $\frac{6}{10}$ in each eye and the visual fields were full. The edges of the discs were blurred and the right disc was swollen

to three dioptres. Rotatory nystagmus was present on conjugate deviation of the eyes to the right. With the exception of slight inco-ordination in the right upper limb, no other abnormality was detected in the central nervous system.

A diagnosis of right cerebellar tumour was made, and a right cerebellar decompression was performed by Sir Victor Horsley on June 28, 1910. The skull was very thin and the dura mater was under great tension. On July 5, the second stage of the operation was undertaken; an encapsuled glistening tumour was seen beneath the right lobe of the cerebellum. The capsule was incised and its contents—white pultaceous matter—were scraped out.

A fortnight later, the wound was discharging purulent material, films of which revealed polymorphonuclear cells with a few pneumococci. In addition, tumour material consisting of cholesterin crystals and large round epithelial cells exuded from the wound. The temperature ranged from normal to 103° F. Six weeks after the operation, the wound looked quite clean and there was only slight discharge, but the temperature remained elevated and glycosuria was present.

The pulse gradually became weaker, the general condition deteriorated and the patient died on September 18, 1910.

No post-mortem examination was made.

Case 6.—Epidermoid at the anterior end of corpus callosum.

A. H., male, aged 20, was admitted to the National Hospital under the care of Dr. Risien Russell, on May 8, 1916, complaining of headache, dimness of vision and drowsiness.

In February, 1916, he had been suddenly taken ill with headache, vomiting and marked rigidity of his neck. A provisional diagnosis of cerebro-spinal meningitis was made and he was admitted to hospital.

The cerebro-spinal fluid, however, was not turbid and no meningococci were found. His condition gradually improved, until, with the exception of a complete right facial paralysis, he appeared to be well again.

On April 28, the headache and vomiting recurred and he complained of severe giddiness.

Condition on admission, May 8, 1916: he was a short, thick-set lad with slow, hesitant speech and a poor memory for recent events. The visual acuity was $\frac{6}{18}$ in the right eye and $\frac{6}{24}$ in the left. There was bilateral papillœdema. The right eye was proptosed, the left external rectus weak and the right lower face was paralysed.

There was weakness of the left arm and astereognosis in the left hand. The tendon reflexes were sluggish, the plantar responses flexor and the abdominal reflexes were present and equal.

The Wassermann reaction in the blood was negative.

Mr. Armour performed decompression operations in the occipital region on August 8 and August 29. A limited post-mortem examination, which was made on August 29, revealed a typical "pearly tumour" in the midline in the

region of the anterior end of the corpus callosum. The histological appearances were those of a true epidermoid.

Case 7.—Epidermoid in the right parietal region.

E. P., male, aged 37, was admitted to the National Hospital under the care of Dr. Gordon Holmes on September 8, 1921, complaining of weakness of the left arm and leg of fifteen months' duration. His previous illnesses included three attacks of rheumatic fever, pneumonia twenty years previously, and an appendicectomy six years ago. The family history was uneventful, except that his father had committed suicide at the age of 50.

History of present illness.—About fifteen years ago he complained of feeling very languid and tired; severe headache appeared and made him dazed and stupid. He found that he made mistakes in his business as a boot salesman. Twelve months ago he found he could not "control" his left leg, and walking became difficult. The leg improved for a month and then relapsed. About this time he collapsed altogether one day; his head was very bad and he became delirious. He remained fourteen days in bed with marked weakness of the left leg and left arm. Following this, he began to have slight attacks without warning, in which things would drop from his hands and he sat limply in a chair with a vacant expression. His memory and general mental condition were very bad at this time, but have improved considerably since. The headaches have become less frequent and severe during the past seven months, but the left arm and leg have grown weaker. Vomiting occurred on one occasion only.

Clinical examination.—Well nourished, pale man, talks slowly and has difficulty in recalling past events. Emotionally, he appears normal. The visual acuity is $\frac{6}{9}$ in the right eye and $\frac{6}{12}$ in the left. The right optic disc appears a little red and the nasal edge is hazy; the left disc is normal. There is a definite defect in the temporal field in the left eye, the left palpebral fissure is wider than the right and the tongue deviates to the right. The left arm is definitely weak, and there is clumsiness in the hand movements of that side. Co-ordination tests are carried out slowly and inaccurately. The left leg is weak in all movements and there is some spasticity on that side.

All forms of sensation are intact except for astereognosis in the left hand. The arm jerks are present and equal; knee and ankle jerks exaggerated on the left side; plantar stimulation gives an extensor response on the left and a flexor response on the right. All the abdominal reflexes are absent.

An X-ray of the skull revealed a somewhat flattened sella turcica, the posterior clinoid processes of which were eroded. The cerebro-spinal fluid contained 62 cells per cubic millimetre, 0·02 per cent. albumin and the Wassermann reaction was negative.

A diagnosis of right-sided parietal tumour was made, and Sir Percy Sargent operated on October 7, 1921. The skull, which was trephined in the region of the angular gyrus, was thin and brittle; the dura mater was under considerable tension. The gyri were nowhere flattened, but felt softer at a point immediately above the angular gyrus. An incision in this region opened a

cyst lying about 1 inch from the surface. A fairly clear but flaky fluid escaped, carrying up with it a large quantity of laminated necrotic material. It could not be ascertained with certainty whether or not the ventricle was opened.

The cyst contents were reported upon as follows: Yellow fluid contaminated with blood; cells—a few lymphocytes; albumin 0·5 per cent., N.A. + +; urea 0·46 per cent. There is an amorphous mass of rounded bodies in the deposit, giving it a whitish appearance.

The patient stood the operation well. Ten days later he became incontinent; the left-sided weakness was obviously greater, he complained of pains all over and a stiffness at the back of the neck. He was very drowsy. Two days afterwards he was completely powerless down the left side. His mental state was retarded and childish. He improved a little, and three weeks from the time of operation he was able to walk with support; the headaches were returning, however, and the hernia cerebri was growing more tense.

The patient died on December 6, 1921, of broncho-pneumonia.

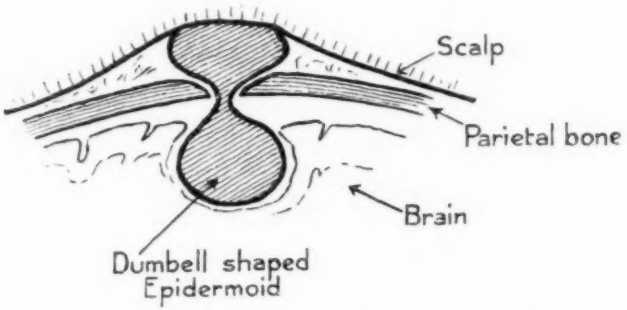

FIG. 10.—Diagrammatic sketch of the tumour in *Case* 8.

During the first three days following the operation the temperature ranged from 99° to 101°F. It then rose to 103°F. and remained elevated for a fortnight. During the following week the temperature was normal on several occasions, but afterwards he ran an irregular fever until death.

Post-mortem note.—The base of the brain, the area from which the tumour was removed, and the lateral ventricles are full of greenish pus. There is practically a solid abscess lying in that part of the brain where the tumour grew.

The histological appearance of the tumour was that of a typical epidermoid (see fig. 4).

Case 8.—Epidermoid of the right parietal region.

A male, aged 76, was brought in dead to the Casualty Department of the Miller General Hospital, Greenwich, in April, 1928. Apparently he had suddenly collapsed in the street. According to his relatives, who included a

medical man, there had been no previous symptoms whatever, either cerebral or circulatory. At the autopsy, an infarction of the heart wall was discovered, resulting from intense atheroma of the proximal portion of the left coronary artery. When the scalp was stripped from the calvarium, a soft boggy swelling was discovered lying in the region of the right parietal eminence. The mass was in intimate connection with the scalp, for it was torn when the scalp was peeled off, giving rise to an escape of yellow grumous matter. Further examination revealed that the mass lay in a circular depression in the parietal bone, and that the outer table had been extensively eroded. In the centre of this depression was a small circular aperture in the inner table, with a diameter of a quarter of an inch. When the skull was opened a second tumour was found lying immediately beneath the cranial perforation and communicating

FIG. 11.—Section through semi-ovale of *Case* 8, showing the tumour lying embedded immediately below the parietal cortex.

with the scalp tumour through the foramen in a dumb-bell fashion (see fig. 10). The intracranial tumour lay beneath the pia-arachnoid and in intimate contact with the cortex of the postcentral gyrus. The brain tissue was pushed aside and appeared to be invaded only at the opposite poles of the growth which were buried beneath the surface of the hemisphere. Cross-section of the brain revealed that the tumour was the size of a walnut and contained a pale-yellowish caseous-like material. There was a definite capsule with a typical mother-of-pearl sheen (see fig. 11).

We have examined these cases and the cases recorded in the literature in an endeavour to determine whether there was any feature by which the nature of the tumour could be forecasted prior to operation, or whether, on recognizing the nature of the tumour at operation, the mode of procedure should be modified. Special attention has been paid to the following points : age, sex, previous history, duration of symptoms, presence of any symptoms other than the general and localizing signs of

an intracranial tumour, the site of the tumour, presence of mental symptoms, and the occurrence of meningitis after operation. For convenience we have tabulated these results below :—

EIGHT CASES OF CEREBRAL EPIDERMOIDS.

Case	Sex	Age	Previous history	Duration of symptoms	Mental state	Site of tumour	Occurrence of "meningitis" after operation
1. H. G. M. ..	Male	27	Good	6 mths.	Normal	L. ponto-cerebellar	Died day of operation
2. T. O'M. ..	Male	28	Good	7 yrs.	Drowsy	R. ponto-cerebellar	Died day of operation
3. C. A. ..	Male	37	Good	2 yrs.	Normal	Mid cerebellar	Localized "meningitis" for two months
4. J. S. ..	Male	28	Many illnesses	3 mths.	Normal	Midline posterior end corpus callosum	Died day of operation
5. M. D. ..	Male	41	Good	19 mths.	Normal	R. extra-cerebellar	Localized "meningitis" for two months
6. A. H. ..	Male	20	Good	3 mths.	Drowsy	Midline anterior end corpus callosum	Died day of operation
7. E. P. ..	Male	37	Many illnesses	15 mths.	Drowsy	R. parietal	"Meningitis" for two months
8. M. . ..	Male	76	Good	No symptoms	Normal	R. parietal	No operation

We would wish to call attention to the following points :—

Sex.—All our cases occurred in the male sex. The occurrence of these pearly tumours is not, however, confined to males. Nevertheless, there does appear to be a more marked preponderance of this type of tumour in the male, when the sex incidence figures are compared with those found in other intracranial neoplasms.

Age.—Seven out of the eight cases occurred in the second and third decades, the average age being 37.

Previous history.—In five out of the eight cases, the patients were very healthy and not abnormal in any way prior to coming under observation with signs of an intracranial tumour. In one case (No. 1) it is interesting to note that, while in the Army, two and a half years before developing other signs, he was frequently being corrected

for holding his head to the left. A tumour in the left ponto-cerebellar angle was found at operation.

In two of the cases there were histories of many illnesses, but nothing to indicate that there was any intracranial lesion.

Duration of symptoms.—It is stated that the tumours are slowly growing, and that, the onset being very gradual, the symptoms are generally of long duration. The average duration of symptoms in the above eight cases was about twenty months—in four of the cases the duration was six months or less.

Mental state.—The earlier writers stressed the frequent occurrence of mental symptoms in cholesteatomata. In none of our cases was the mental state grossly affected; in three cases there was slowness of cerebration and general mental dulling, but not in excess of what one might expect in a patient with an intracranial tumour. We feel that mental symptoms were probably more pronounced in the earlier recorded cases, because operation was then postponed for a much longer period or not undertaken.

The site of the tumours.—In our eight intracranial cases, four were extra-cerebellar, two were in the right parietal region and two in the midline in relation to the corpus callosum. The problem of the favourite sites of the tumours has been dealt with in an earlier paragraph.

From a careful examination of our own cases and those recorded in the literature, we are unable to find any pre-operative features, symptoms or signs which are peculiar to cholesteatomata.

The occurrence of "meningitis."—The occurrence of localized "meningitis" after operation has been noted frequently in cholesteatomata. In three out of seven of our patients who underwent operation, there was evidence, both clinical and pathological, of a post-operative meningeal irritation. In two of the cases the "meningitis" appeared to be localized to the operation area; there was no evidence of a general meningitis. In the third case, E.P., in which a large cyst, full of flaky fluid and laminated necrotic material, had been found in the right parietal region, and in which it was doubtful whether the ventricle had been invaded or not, greenish pus was found at autopsy in the cyst cavity and in the lateral ventricles. In all three cases the patient survived the operation for approximately two months with similar symptoms—drowsiness and irritability, neck stiffness, pains over the body, and gradual deterioration. Of the other five cases, four unfortunately died within forty-eight hours of operation, and in one case operation was not undertaken.

It is difficult to be certain of the exact nature of the pathological change which occurs locally in some of these "cholesteatomata" after an attempt has been made to remove them. There is no definite evidence, from examination of the cerebro-spinal fluid, that it is an infection. It would appear rather to be an irritation of the meninges set up locally by toxic material contained within these tumours. Furthermore, it is of sufficiently frequent occurrence to call for excessive care in the removal of the tumour, in order to prevent the contamination of the neighbouring structures with the toxic contents.

Spinal Epidermoids.

We have been fortunate enough to observe a case of an epidermoid of the spinal canal. The occurrence of this type of tumour in this situation is distinctly rare; Percival Bailey, in 1920, in discussing the location of pearly tumours, mentions the fact that Chiari described a case in which the tumour was found in the spinal canal.

Previous cases of dermoid and epidermoid tumours of the spinal canal.—The earliest reference which we have been able to obtain concerning spinal tumours of this nature is to a case recorded by Eppinger in 1875. In this case there were multiple tumours of the cord and brain, apparently growing in relationship with the blood-vessels.

In 1883, Chiari [10] reported an intramedullary cholesteatoma in a man, aged 33, who had been regarded as a case of transverse myelitis for nineteen years. The tumour was 4 cm. in length, and lay at the level of the fourth to sixth dorsal segments, chiefly in the region of the central canal of the spinal cord, but it extended outwards at one point to come into contact with the pia mater. There were no associated malformations of the spinal column.

Ten years later Muscatello [39] described the condition found in a female infant, aged 5 months. There were some "cholesteatomatous perles" in addition to a dermoid, lying extradurally and adherent to the periosteum at the level of the fifth lumbar vertebra. A bifid thoracic spine was present in this case.

In 1898, Trachtenberg recorded the case of a man, aged 55, who had complained for four years of symptoms of a transverse myelitis. At post-mortem, multiple arachnoidal epidermoids and dermoids were found in relation to the arachnoid of the cervical, dorsal and lumbar portions of the cord. In addition, cholesteatomata were found in the left Sylvian fossa, in the left frontal lobe, in both lateral ventricles, in the choroid plexuses of the lateral and third ventricles and in the

corpora quadrigemina. There were no associated malformations of the spinal column.

Microscopically, he stated that they resembled the tumours described by Bostroem ; epithelial tissue was found in one tumour, but no hair was present.

Further cases were recorded by Ivanoff [22] in 1903, and Raymond, L'Alquier and Courtellemont in 1904. In the latter case, which occurred in a male aged 34, the spinal lesion was associated with dermoids in the right frontal lobe and in the pituitary region. The patient commenced to suffer with headache and vertigo and loss of memory two years before his death. Later he had a fit and developed a spastic gait. The cerebrospinal fluid was then normal. Three months later headache and vomiting recommenced ; the cerebro-spinal fluid then showed on centrifugalization a layer of amorphous matter 2 cm. deep, staining black with osmic acid and bluish with hæmatin. On post-mortem examination a tumour in the right frontal lobe was seen which consisted of a milky mass with strands of hair in it. Histologically, the tumour stained black with osmic acid, and there was an epithelial appearance in its wall. Small nodules were present on the spinal cord, in relation to and connected with the pia mater. The spinal cord and brain lesions were similar, and the case was probably one of multiple dermoid cysts.

In 1906, Berka [6] described a tumour—probably a dermoid—which was found in the medullary cone. It was lying in the substance of the spinal cord, dorsal to the central canal ; its capsule was in relation to the pia mater. There were no associated malformations of the spinal column. The patient was a woman, aged 27, who had complained of symptoms of a transverse myelitis for eight years.

A pial dermoid—the tumour was attached to the pia by connective tissue—was reported by Harriehausen [18] in 1909. There was a history of symptoms of a transverse myelitis of nine years' duration given by this patient, who was a woman, aged 23. Doubling of the cord was found below the tumour.

Verébély [57], in 1913, related an interesting case in a 15-year-old boy, who had a spina bifida occulta and from whom a congenital tumour in the lumbar region had been removed. The tumour consisted of two cysts, the size of apples, united by a stalk 2 cm. long ; the one was connected with the dura mater, the other with the skin. The contents were thick, rich in cholesterin and contained fine hair. The wall of the outer cyst was thick and consisted of connective tissue, lined by

flattened epithelium ; the wall of the inner cyst was thinner and lined by epithelium with small papillary excrescences. There was no epithelium in the connecting stalk, which consisted of a loose connective tissue framework with numerous blood-vessels.

Willy Lauterburg's case [28], published in 1922, was an epidermoid in the subdural space and cauda equina, occurring in a boy aged 7. At the age of twenty-two months this child had "acute brain inflammation." The illness had commenced with cramps, vomiting and high fever; this was followed by marked drowsiness, paralysis of the left seventh nerve strabismus, inequality of the pupils, and slight paresis of the left arm. Lumbar puncture showed a turbid fluid containing lymphocytes, and the case was diagnosed as one of tuberculous meningitis. Two months later the child left hospital apparently cured. In September, 1918, when the child was 7 years old, it suddenly became ill again, abnormal coldness and vomiting being prominent symptoms. Later he developed a total flaccid paralysis with Cheyne-Stokes breathing, and died a few days later from heart failure. Lumbar puncture showed seventy cells per cubic centimetre, of which 23 per cent. were polymorphonuclears At the autopsy, there was a slight internal hydrocephalus, and an old softening in the head of the right caudate nucleus. Foci of encephalitis were found in the pons. A mother-of-pearl tumour, measuring 12 cm. by 10 cm. by 8 cm., of elastic consistency, easily cut, and with flattened poles, was found in the subdural space in the region of the cauda equina. With the exception of a minute vascular pedicle, the tumour lay free between the arachnoid and the dura mater. On transverse section the periphery of the tumour was lamellated, and the centre was yellowish ; a small portion of it showed an epidermal membrane.

The eleventh case was reported by Marinesco and Draganesco in 1924 [35]. A male, aged 30, was admitted to the hospital in August, 1923, with a history of progressive weakness of the legs, left more than the right, of eight and a half years duration, together with some sphincter trouble. In August, 1916, a soft tumour, a cholesteatoma, was found lying under the dura mater ; its extent and relations were doubtful. Two months later he could stand. In 1920 he fell and became worse again ; in 1921 he was readmitted to hospital. At this time sensibility was lost up to the tenth dorsal segment and there was a band of hyperalgesia, stretching from the sixth to tenth dorsal segments. There were bilateral extensor plantar responses and exaggerated tendon jerks. He died in November, 1923, as a result of septicæmia. At autopsy, tumefaction with a cystic cavity was found at the level of the

tenth and eleventh dorsal segments. The dura mater and leptomeninges were incorporated in the walls of the cyst. The cyst contained a yellow detritus and cholesterin crystals—plaques of cholesterin were attached to the arachnoid. There was degeneration of the posterior columns in the cord above the tumour; below the tumour the cord was normal.

In the present state of our knowledge of the pathology of these epidermoid and allied tumours, and in view of the difficulties which have confronted us with regard to terminology, we have been in doubt as to how many cases of true "epidermoids" of the spinal canal have been recorded. In several of the cases which we have reviewed the pathological data have been insufficient to enable us to state their exact nature (cases of Eppinger and Ivanoff). It is probable that most of them are dermoid tumours. The cases recorded by Raymond, Alquier and Courtellemont, Berka and Harriehausen are almost certainly dermoids and probably also those reported by Muscatello and Verébély.

However, the lesions in the cases described by Chiari, Trachtenburg, Lauterburg and Marinesco and Draganesco are possibly true epidermoids. Bostroem examined a section of the tumour from Chiari's case and pronounced it a typical epidermoid. Trachtenburg said that microscopically his tumour resembled those described by Bostroem, but also states that fat and sweat glands were definitely present.

Case 9.—Epidermoid of the spinal canal.

N. E., male, aged 15, was admitted to the National Hospital under the care of Dr. Gordon Holmes, on July 7, 1927. He complained of weakness and stiffness of both legs of four months' duration. The family history was good.

He was a normal child at birth, but, when 3 years of age, he had an attack of cerebro-spinal meningitis. The onset of this illness was very sudden, with rigors, vomiting and unconsciousness. He was "unconscious" for seventeen weeks, and during that time repeated lumbar punctures were performed and many injections of anti-meningococcal serum were given. However, he made a complete recovery; there were no ocular or aural defects and no mental retardation.

He remained well and strong until the age of 7, when he commenced to limp. He had no acute illness at the time, but the legs became weaker and weaker until two or three months later he was unable to walk or even stand. After twelve months' treatment with massage and electricity, he began to improve, and within eighteen months he was walking almost normally again. From that time until April, 1927 (aged 15), he was perfectly well, save that he limped slightly on his left leg and the left foot was everted.

Mentally, he was considered a normal child, and he progressed well at school. He had no other illnesses.

In April, 1927, he was in bed for three weeks with an attack of influenza, and during that time he complained of a severe ache in his legs. When he was allowed to get up again, he found that he was unable to stand or walk without assistance. There was no disturbance of the sphincters.

On examination, he was a pale-faced, bright, cheerful boy. The cranial nerves and upper limbs were normal. Both legs were spastic and weak; there was a definite sensory level at the eighth dorsal segment. The knee and ankle jerks were grossly exaggerated; the abdominal reflexes were absent and the plantar responses extensor. The patient was able to take two or three steps when supported on both sides. Scoliosis in the lower dorsal region was present, otherwise the spine appeared normal. The report on the cerebrospinal fluid was as follows: Slightly yellow, no coagulum, three cells per cubic millimetre, total protein 1 per cent.; globulin tests were positive, but the Wassermann reaction was negative. An X-ray of the spine demonstrated the presence of scoliosis but no other abnormality.

On July 14, 1927, Sir Percy Sargent performed a laminectomy in the mid-dorsal region. On removing the laminæ of the seventh and eighth dorsal vertebræ, the tumour was brought into view. It was yellowish-white in colour, soft in consistency and like very fine sago compressed into a mass. The surface was a dull mat and consisted of innumerable fine scales, which fell off when the surface was flicked. The interior of the tumour was composed of similar scales, but they were moister and glued together. The mass was not enclosed in a capsule, and the greater portion of it was extracted piecemeal. Histologically this was a true epidermoid (see fig. 2).

It was difficult to be certain of the exact relation of the tumour to the meninges, but it was certainly subdural and intimately bound up with the pia-arachnoid. A temperature of 99·2° F. was recorded on the day following the operation; otherwise there was no pyrexia, and the patient made a good recovery.

On discharge from the hospital on December 21 he was able to walk with a little assistance and there was some return of sensation. He wrote to us on May 8, 1928, saying: "The muscles of the legs are now of normal size and the right leg is very strong. I can walk around the house and up and down stairs by myself; in addition, I can walk about one hundred yards with the aid of sticks. The feeling in my legs is the same now as when I left the hospital. My general health and appetite are excellent."

It is interesting to note that there was no evidence that any local meningeal reaction followed the laminectomy, despite the fact that the tumour had to be removed piecemeal.

N. E. gave a history that at the age of 3 he had an illness called "cerebrospinal meningitis," from which he made a complete recovery. At the age of 7, for some unexplained reason, his legs gradually became weaker until he was unable to walk. He again made an almost complete recovery, and remained well for eight years, when the symptoms returned. When we compare this with the histories of the previously

reported cases, we find that the child recorded by Lauterburg had an illness called "tuberculous meningitis" at the age of 22 months, from which he made a complete recovery, and that Marinesco and Draganesco's patient remained fairly well and able to walk for four years after the cholesteatoma was revealed at operation.

The microscopical section showed the tumour to be a true epidermoid with a broad epithelial layer.

Summary.

A study of the cases recorded in the literature makes it obvious that the problem presents many points of confusion and uncertainty. First, the term "cholesteatoma" has been made to apply to several entirely different types of growth; secondly, the nature and sites of origin are disputed points; and, thirdly, there is no uniform nomenclature.

The term "cholesteatoma" has been at various times applied not only to new growths lying in the median excavation of the brain, with a more or less close leptomeningeal attachment, but also to numerous other tumours of such diverse nature as the products of chronic otitic inflammation, ventricular neoplasms in the horse, tumours growing within the skull bone and cholesterin-containing cysts in the region of the infundibulum. Some other tumours, which have by various authors been named cholesteatomata, are certainly dermoids; others are obviously endotheliomata.

The cerebrospinal cholesteatomata, properly speaking, are essentially epithelial growths, which arise not by a metaplasia of arachnoidal cells, but from embryonic cell inclusions. They are allied to the dermoids, but differ in containing tissue elements which are entirely ectodermal. "Cholesteatomatous-endotheliomata" are probably tumours of an entirely different nature.

Various reasons are given for the employment of the term "epidermoid" in lieu of the less definitive and ambiguous expressions, "pearly tumour" or "cholesteatoma."

Details of eight personal cases of intracranial epidermoids are given. In spite of a careful search for any distinguishing clinical features, the results have been negative; the nature of the symptomatology appears to depend solely upon the *site* (as opposed to the *nature*) of the growth.

One personal case of spinal epidermoid is recorded.

In conclusion we beg to thank the physicians and surgeons of the National Hospital, Queen Square, for permission to make use of their cases. Our grateful thanks are also due to Dr. Greenfield, Dr. Weston Hurst and Professor Tom Hare for their kind assistance.

BIBLIOGRAPHY.

[1] ADAMS, W. "Cholesteatomatous Tumour of the Brain." *Trans. Path. Soc. Lond.*, 1850-51. **3**, 44.

[2] BAILEY, P. "Cruveilhier's 'Tumeurs perlées,'" *Surg., Gyn. and Obst.*, 1920, **32**, 390.

[3] *Idem.* "Further Observations on Pearly Tumours," *Arch. Surg.*, 1924, **8**, 524.

[4] BENDA, C. "Zwei Fälle von Cholesteatom des Gehirns," *Berl. klin. Woch.*, 1897, **34**, 167.

[5] BENEKE. "Ueber der Histogenese der pialen Cholesteatome," *Schmidt's Jahrb.*, 1897, **256**, 116.

[6] BERKA. "Cholesteatom der Cauda Equina," *Casopis lekaruv Ceskych.*, 1906, No. 11.

[7] BLAND-SUTTON, J. "Orations and Addresses." London: Heinemann, 1924. No. IX.

[8] BLUMER, G. "Bilateral Cholesteatomatous Endotheliomata of the Choroid Plexus." *Johns Hopkins Hosp. Rep.*, 1900, **9**, 279.

[9] BOSTROEM, E. "Ueber die pialen Epidermoide, Dermoide und Lipome, und duralen Dermoide," *Centralbl. f. allg. Path. u. path. Anat.*, 1897, **8**, 1.

[10] CHIARI. "Centrales Cholesteatom des Dorsalmarkes mit volkommen entwickelten auf- und absteigender Degeneration," *Prager med. Wochenschr.*, 1883, **142**, 429.

[11] CRUVEILHIER. "Anatomie pathologique du corps humain," vol. i, book 2, plate 6.

[12] CUSHING, H. "A Large Epidermal Cholesteatoma of the Parieto-occipital Region deforming the Left Hemisphere, without Cerebral Symptoms," *Surg. Gyn. Obstet.*, 1922, **34**, 557.

[13] DUMERIL. *Bull. de la Soc. Faculté de Méd.*, 1807, **2**, 32.

[14] FRANK, C. "Ueber einen in der Duerener Irrenanstalt beobachteten Fall von Cholesteatom," *Allg. Zeitschr. f. Psych.*, 1890, **46**, 30.

[15] FRANK, H. "Ein Fall von Cholesteatom der weichen Hirnhäute," Inaugural Dissert., Marburg, 1892.

[16] GLAESER, E. "Untersuchungen über Cholesteatome und ihre Ergebnisse für die Lehre von der Enstehung des Geschwülste," *Virchow's Arch. f. path. Anat.*, 1890, **122**, 389.

[17] GREENFIELD, J. G. "Cholesteatoma in the Ponto-Cerebellar Angle," *Proc. Roy. Soc. Med.* (Neur. Sect.), 1921.

[18] HARRIEHAUSEN. "Ueber Dermoide im Wirbelkanal neben Verdoppelung des Rückenmarkes," *Deutsch. Zeitschr. f. Nervenheilk.*, 1909, **36**, 268.

[19] HARVEY, S. C., and BURR, H. S. "Development of the Meninges," *Arch. Neurol. and Psych.*, 1926, **15**, 545.

[20] HORRAX, G. "A Consideration of the Dermal *versus* the Epidermal Cholesteatomas having their Attachment in the Cerebral Envelopes," *ibid.*, 1922, **8**, 265.

[21] HUMISTON, C. E., and PIETTE, E. C. "True Cholesteatoma of the Cæcum," *Journ. Amer. Med. Assoc.*, 1921, **84**, 874.

[22] IVANOFF, N. J. "Cholesteatom des Rückenmarks," *Journ. Neuropat. i Psikhiatri Korsakova*, Mosk., 1903, iii, Suppe S., 280.

[23] KAKESHITA, T. "Zur Pathologie der Hirn-Cholesteatome," *Arb. r. d. Neurol. Inst. a. d. Wien. Univ.*, 1925, **27**, 327.

[24] KARLEFORS, J. "A Contribution to the Question of the Genesis of the Cholesteatoma in the Temporal Bone and its Operative Treatment," *Acta Oto-laryng.*, 1925, **8**, 417.

[25] KAY, F. A., and PACK, G. T. "Cholesteatoma of the Brain," *Arch. Neurol. and Psych.*, 1928, **34**, 557.

[26] KLEBS, G. "Die allgemeine Pathologie," Jena, 1889, vol. ii, 627.

[27] KUTVIRT, O. "De l'agrandissement de la cavité cholestéatomateuse," *Acta Oto laryng.*, 1925, **8**, 517.

[28] LAUTERBURG, W. "Ein Epidermoid frei im Wirbelkanal und seine Kombination mit Hirnläsionen," *Virchow's Arch. f. pathol. Anat. u. Physiol.*, 1923, **240**, 328.

[29] LE PRESTRE. "Tumeur adipociriforme dévelopée dans le mésocéphale," *Arch. gén. de Méd.*, 1828, **18**, 19.

[30] LOCKWOOD, B. C. "Cholesteatomatous Cystic Tumour of the Pituitary Gland," *Journ. Amer. Med Assoc.*, 1921, **76**, 1218.

[31] MCCARTHY, D. J. "Cholesteatoma vasculosa of the Choroid Plexus of the Lateral Cerebral Ventricles," *Proc. Path. Soc. Philad.*, 1904, **7**, 233.

[32] M'Fadyean, J. "Cholesteatoma in the Brain of a Horse," *Journ. Comp. Path.*, 1902, **15**, 161.
[33] *Idem.* "Cholesteatoma in the Brain of a Horse," *ibid.*, 1911, **24**, 137.
[34] Marie, P., et Roussy, G. "Un cas de cholestéatome de la base de l'encéphale," *Rev. Neurol.*, 1905, **13**, 1183.
[35] Marinesco, G., et Draganesco. "Kyste épidermoide cholestéatomateux de la moelle épinière coexistent avec un processe syringomyélique. Contribution à l'étude de la syringomyélie," *ibid.*, 1924, **31**, ii, 338.
[36] Martin, J. F., Dechaume, J., et Puig. "Morphologie et histogenèse des tumeurs méningées craniennes," *Annales d'Anat. path.*, 1928, **5**, 277.
[37] Meyer, W. R. "Zur Kasuistik der epidermoidalen Cholesteatome des Gehirns," *Virchow's Arch. f. pathol. Anat. u. Physiol.*, 1913, **211**, 161.
[38] Müller. "Ueber den feineren Bau und die Formen der krauschaften Geschwülste," 1838, 50.
[39] Muscatello. "Ueber die angeborenen Spalten des Schädels und der Wirbelsaule," *Arch. f. klin. Chir.*, 1894, **47**, 162 and 257.
[40] Nehrkorn. "Ein Fall von meningealer Perlgeschwulst.," *Beitr. z. path. Anat. u. allg. Path.*, 1897, **21**, 73.
[41] Peacock. "Cholesteatomatous Tumour of the Brain," *Trans. Path. Soc. Lond.*, 1853-54, **5**, 21.
[42] Perls. "Lehrbuch der allg. path. Anat.," 1877, vol. i. p. 486.
[43] Peyrot, M. "Tremblement mercuriel, sudamina. Tumeur comprimant le cervelet," *Arch. gén. de Méd.*, 1834, **4** (2me série), 620.
[44] Pollitzer. "Diseases of the Ear," 6th Edition, 1926.
[45] Price, J. A. P. "Cholesteatoma at the Base of the Brain," *Trans. Path. Soc. Lond.*, 1886-87, **38**, 24.
[46] Raymond, F., L'Alquier et Courtellemont, V. "Un cas de kyste dermoïde des centres nerveux," *Rev. Neurol.*, 1904, **12**, 635.
[47] Roussy, G., et Cornil, L. "Tumeurs cérébrales," *Nouv. Traité de Méd.*, fasc. 19, 526.
[48] Rutherford, C. "Some Cases of Brain Disease," *Journ. Comp. Path.*, 1893, **6**, 72.
[49] Schmaus, H. "Grundriss der pathol. Anat." Wiesbaden, 1910, p. 241.
[50] Scholtz. "Einige Bemerkungen ueber das meningeale Cholesteatom in Anschluss an einen Fall von Cholesteatom des III Ventrikels," *Virchow's Arch. f. path. Anat.*, 1906, **184**, 225.
[51] Schulgin. Quoted by Meyer, W. R.
[52] Shefferd, J. "Cholesteatoma of the Temporal Bone, with the Report of an Unusual Case," *Boston Med. and Surg. Journ.*, 1922, **186**, 877.
[53] Stevenson, G. F. "A Case of Paralysis due to Psammoma," *Veterin. Journ.*, 1923, **79**, 32.
[54] Thoma. "Textbook of General Pathology and Pathological Anatomy" (English Edition), London, 1896, p. 578.
[55] Tooth, H. H. "The Treatment of Tumours of the Brain," *Proc. XVIIth Internat. Congr. Med.*, Lond., 1913, Sect. XI, p. 252.
[56] Trachtenberg, M. A. "Ein Beitrag zur Lehre von den arachnoidealen Epidermoiden und Dermoiden des Hirns und Rückenmarks," *Virchow's Arch. f. pathol. Anat. u. Physiol.*, 1898, **154**, 274.
[57] Verébély, T. V. "Ein Fall von intravertebralen Dermoidzyste," *ibid.*, 1913, **213**, 541.
[58] Verattus. "De Bononiensi Scientiarum et Artium institute atque academia commentarii," 1745, vol. ii, pt. 1.
[59] Virchow. "Ueber Perlgeschwülste," *Virchow's Arch. f. path. Anat.*, 1855, **8**, 371.
[60] Wilkinson, G. "Two Cases of Cholesteatoma of Unusual Size extending into the Posterior Fossa and causing Obliteration of the Sigmoid Sinus," *Proc. Roy. Soc. Med.* (Otol. Sect.), 1910, **3**, 82.
[61] Wilks. "Two Cases of Cholesteatomatous Tumour of the Brain," *Trans. Path. Soc Lond.*, 1858-59, **10**, 24.
[62] Wyatt Wingrave, V. H. "Notes on the Pathogeny of Cholesteatomata," *Proc. Roy. Soc. Med.* (Otol. Sect.), 1910, **3**, 63.

THE SYMPTOMATOLOGY OF TUMOURS OF THE TEMPORAL LOBE.

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THE difficulty in localizing tumours of the temporal lobe, especially of the right, is generally recognized, but the possibility of resection of a large portion of the right, and even of the left, temporal lobe without noticeable functional disturbance, makes an early localization of a temporal lobe tumour imperative. It is in early stages of tumours of the temporal lobe that even the last resort of neurological diagnosis—ventriculography—gives occasionally no clue as to the localization.

The literature dealing with the diagnosis of temporal lobe tumours has grown considerably since the appearance of Knapp's monograph [11] over twenty years ago. This monograph was the more important since only eight years previously Oppenheim [15] stated: "Wir haben niemals das Recht die Lokaldiagnose Tumor des rechten Schläfenlappens zu stellen." The literature that followed Knapp's contribution has added to our knowledge of the symptomatology of these tumours, but, on the other hand, it has obscured the importance of certain signs pointed out by Knapp. This discrepancy is easily understood when one realizes the intermittent character of many symptoms in the course of an intracranial tumour. It is a fact that many a symptom is present and is of diagnostic significance only during a certain phase of the development of the tumour.

Temporal lobe tumours are not frequent, and it is significant that none of the contributions dealing with the symptomatology of these tumours which has appeared up to date is based on more than a dozen cases; many of these contributions have behind them only single instances. Conclusions drawn from such a limited material are apt to be erroneous, especially if the importance of a certain symptom is emphasized or denied, for no single sign or symptom can always establish localization.

Three stages may be distinguished in the natural history of an intracranial tumour: (1) when there are no signs or symptoms;

(2) when local signs and symptoms are present, and (3) when general signs and symptoms complete the picture. A systematic examination of the symptoms of temporal lobe tumours during their entire course is essential if one is to learn of their value in localization. It is with this idea in mind that I have studied a series of thirty-eight cases of tumours confined to the temporal lobe of patients of the National Hospital, Queen Square, London. The value of this material is enhanced by the fact that all these cases were observed and studied by the same methods, and most of them by the same members of the staff. A correlation of the symptoms and signs presented by these tumours with the anatomical lesions is essential for evaluation of the rôle of the former in the symptom-complex of the neoplasm, and therefore I have selected for this study only cases in which a post-mortem examination permitted study of the gross anatomical features.

Physiologically and pathologically the various phenomena composing the symptom-complex of an intracranial tumour are interdependent, and interwoven to a great degree. However, for purely didactic purposes one may with benefit subdivide them into those resulting from intracranial pressure, from irritation of the neighbouring areas of the brain, and, thirdly, from focal destruction of the involved region. There were seventeen tumours of the right and twenty-one tumours of the left temporal lobe. From a detailed study of the symptomatology of these thirty-eight cases I shall attempt to show the characteristic neurological picture of tumours of the temporo-sphenoidal lobe, the relative value of the various symptoms and signs, and the diagnostic points that serve in the differentiation of a tumour of the right temporal lobe from one in the left lobe. There were twenty-six male patients and twelve female. The average age for the entire series was 47 years; of the male patients 48 years, and of the female 43 years. In the male the ages varied between 29 and 60, and in the female between 29 and 62.

Headache.— Being a symptom of general increased intracranial pressure, headache has received little attention in the study of the symptomatology of temporal lobe tumours. Kennedy states that the nature of headaches is "little more than useless" as regards its localizing value; Niessl v. Mayendorf [14] and B. Sachs [18] have suggested that a definitely localized pain or tenderness on percussion of the temporal region may be a focal symptom. In an analysis of the localizing value of headaches it is important to distinguish between headaches and pain in the head, the first being more or less generalized,

while the latter is a definitely localized sensation referred to the skull and scalp.

Every patient complained of headache, which preceded the admission to hospital by varying lengths of time, ranging from one week to two years, the average being about six months. While the severity of the headaches varied in most cases, they followed a definite course. Early in the disease a sudden jerk of the head or stooping was enough to bring on a sensation of fullness or an actual headache which, however, passed off immediately. Later the headaches appeared in severe bouts, lasting one or several days, and they were followed by complete remissions for days, weeks, or even months. With the advance of the disease headaches became constant, but they were of a more dull character, an occasional throb, mostly in the early morning.

When the headaches were general they appeared first, in order of frequency, in the frontal region, behind the eyes, in the occipital region and occasionally in the vertex. In eight cases the headaches were localized and limited to the side of the tumour. A study of the pathological findings in these cases gave no explanation of this localization. The anatomical basis of headaches in raised intracranial pressure remains obscure; the widely accepted view that the nerves of the dura mater are responsible for it, if it holds true at all, is hardly sufficient to explain the "early morning" exacerbations. It is in the early hours of the morning that the formation of cerebro-spinal fluid is at its highest, and the "early morning" headache may be immediately relieved by a ventricular tap. The not unusual complaint of the patients that the headache "comes from the back of the head, pushes forwards and rests with unusual force against the forehead and behind the eyes," would tend to suggest their origin within the ventricular system, possibly in the choroid plexuses.

Pain or local tenderness of the head was observed in ten cases; with two exceptions this was localized on the side of the lesion. In an exceptional case a right-sided temporal lobe tumour involved the thalamus and produced spontaneous pain on the entire contralateral side of the body. In another, a right-sided tumour caused an enormous left unilateral hydrocephalus with tenderness over the left parietal region and left frontal headache. In the remaining eight cases the pain was limited to the ipsilateral side of the face and head. In two left-sided tumours with erosion of the bony floor of the middle cranial fossa on the left side, the patient complained of painful fullness of the cheek, which was accompanied by definite tenderness slightly above the middle

of the left zygoma. In one case of a left-sided basal tumour which herniated through the widened foramen ovale and pressed directly on the third branch of the fifth nerve, the patient suffered with sharp, shooting pains in the mouth and left side of the face, which were especially severe when the headache increased. In the other four cases a dull pain in the scalp appeared, at first only when the patient was lying on the side of the tumour, but later became persistent. However, in three instances the patients preferred to lie on the side of the tumour while in bed. In all cases local pain preceded the appearance of headaches by months, on an average by about five months.

Vomiting.—Vomiting was a symptom in nineteen patients at one time or another, while in the other half vomiting never occurred. As a rule the appearance of vomiting followed that of headaches after a considerable length of time. Vomiting usually came on in almost daily attacks and then disappeared for weeks or months, or even altogether. The dependence of vomiting upon the severity of the headaches is well established; it usually occurred during the early morning hours when the headaches were at their worst. The intervals between the attacks of vomiting usually coincided with the intervals between the bouts of headaches, but it was not a constant accompaniment of headaches. The so-called "projectile" type of vomiting was rarely observed in this series of cases, and in my experience it is not frequently seen in patients with gradually increasing intracranial pressure. In several instances vomiting was occasionally preceded by disagreeable sensations of smell and taste, which were components of an uncinate seizure.

Papillœdema.—In five instances no changes were seen in the fundi on the admission of the patient to, or during his stay in, the hospital: in all the other cases the discs showed definite œdematous changes. In no case did the swelling measure more than 7 D., the average being about 3·5 D. The controversy of some twenty years ago as to the value in localization of the comparative degrees of swelling of the ipsilateral and contralateral discs is still alive to-day; the findings in this series of cases indicate that the relative amount of swelling of the two papillæ is of no value as a localizing sign. In eight left-sided tumours and seven right-sided the amount of swelling was identical in the two eyes. In seven tumours of the left side the swelling of the left disc was greater than that of the right, and in two cases the swelling was less on the left than on the right side. In six tumours of the right lobe the swelling was greater on the right, and in one instance it was greater in the left. Paton [16] has pointed out the unreliability

of the relative amount of swelling of the discs in lateralizing a tumour, but Horsley [7] attached great importance to it; both supported their contentions with clinical observations.

In the estimating of the relative changes in the fundi one must take into consideration, not alone the papillary swelling but also the hæmorrhages and exudate when these are present. Another source of error lies in too short observation of the changes; from a single examination it is impossible to draw trustworthy conclusions since the degree of swelling of the nerve head may change. In a patient with a right-sided tumour, for instance, ophthalmoscopic examination revealed 2·5 D. swelling in the right eye and 3 D. swelling in the left, but two weeks later the same observer (Dr. Gordon Holmes) found a swelling of 4·5 D. in the right and 3·5 D. in the left; while a second patient with a left-sided tumour showed at the first examination 3 D. of swelling in the right and 3·5 D. in the left eye; next week the same measurements were obtained, but two weeks later the same observer found 3·5 D. of swelling in the right and 2 D. in the left papilla. A careful digest of the records suggests that only a comparison of the incipient signs of papillœdema, that is blurring of the edges of the disc with fullness and tortuosity of the veins, is of importance in the lateralization of the tumour, since they may be found at first in one eye only. When the tumour is far advanced the degree of swelling is usually identical on the two sides, and in the late stages one frequently observes more swelling in the eye contralateral to the site of the tumour. The latter is probably due to retrograde degeneration and atrophic changes in the papilla of the ipsilateral eye where the œdema is of longer standing.

Incontinence.—Tumours of the temporal lobe differ from frontal lobe tumours as regards sphincter disturbances. In a series of thirty frontal lobe tumours controlled by autopsy which I have studied, incontinence was observed in 60 per cent., while in the present series of tumours of the temporal lobe it occurred only in 20 per cent. of the cases. The reaction of the patient towards the incontinence is different in the two series: while in temporal lobe tumours the patient is usually ignorant of the incontinence, a patient with a tumour of the frontal lobe realizes the entire act but cares nothing about it; his judgment of its impropriety is impaired. Incontinence is a much earlier symptom in frontal than in temporal lobe tumours, in which it appears only in the late stages of the illness. While no definite conclusions can be drawn from the influence of the seat of the tumour upon the presence

of incontinence, it is of interest that in all eight cases with incontinence as a definite symptom the tumour was situated at or about the pole of the temporal lobe, extended towards the basal ganglia, and occasionally also pressed upon the frontal lobe. An investigation of these eight cases of temporal tumour indicates that complete incontinence is as a rule preceded by frequent and precipitate micturition; but in one instance incontinence was immediately preceded by retention of urine, which persisted for three weeks.

Psychic disturbances.—Psychic disturbances are of little diagnostic value in intracranial tumours in general, and in tumours of the temporal lobe in particular. They may be the result of prolonged increase of intracranial pressure, or they may accompany destructive lesions of various areas of the brain. In their treatises on the symptomatology of temporal lobe tumours, Knapp [10, 11] and Kennedy [9] analysed the psychic disturbances observed from two opposite angles. While Kennedy subordinates all the psychic disorders to the so-called "dreamy state," Knapp includes them all under the term "Korsakow's symptom-complex."

The usual psychic disturbances observed in temporal lobe tumours are loss of memory and changes in temperament and character; they differ greatly from the "dreamy states." While the latter are temporary, more or less periodical alterations of consciousness coming on in attacks, the true psychic disturbances are more or less progressive, or at least stationary, manifestations accompanying the disease. Dreamy states are epileptic equivalents and will be dealt with under the heading "fits."

From the findings in this series of cases I am inclined to group the psychic disturbances as follows: (*a*) Defects of memory, (*b*) change of character and temperament, (*c*) hypersomnia, and (*d*) mental confusion. In 19 patients out of the 38 of this series there was definite subjective, or subjective and objective, evidence of deterioration of memory. This is an unexpectedly high incidence, especially when compared with my series of 30 frontal lobe tumours where changes in memory were definite in 13 cases only. In tumours of the temporal lobe loss of memory is a much later symptom than in frontal tumours, for while in the former it appeared on an average two months before admission to the hospital, in frontal tumours the average was six months. No definite relationship could be made out between defects of memory and the precise site of the tumour in the temporal lobe. The nature of the memory defects in temporal lobe tumours is in some respects different

from that in tumours of the frontal lobe. While in the latter the defects concern only recent events, in temporal lobe tumours it is not unusual to find loss for both recent and past happenings. When failure of memory for past events is observed, it is usually accompanied by slow cerebration and inattention; one is tempted to believe that there is not sufficient will power to recall the past.

The opinion has been expressed in the literature that the psychic disturbances in organic disease of the temporal as well as of the frontal lobe are found mainly with lesions of the left side of the brain. Some authors go so far as to say that psychic disturbances associated with tumours of the right frontal or temporal lobe are merely a result of general pressure. An analysis of the findings in the cases I have studied shows that defects of memory were present in 41 per cent. of the tumours of the right temporal lobe and in 57 per cent. of the left-sided cases, while failure of memory was seen in 38 per cent. of the cases with tumours in the right frontal lobe, and in 47 per cent. of those with left-sided lesions. At a first glance these figures would seem to support the above contention, but a similar analysis reveals changes in temperament and character in 24 per cent. of tumours of the right temporal lobe and 19 per cent. of tumours of the left lobe; in 54 per cent. of tumours of the right frontal lobe, and 53 per cent. of cases with a left frontal lobe tumour. This prevalence of defects of memory in tumours of the left side as compared with tumours of the right side of the brain is, I believe, due to the frequency of speech disturbances in disease of the left temporal and frontal lobes. Memories are largely auditory and visual impressions, but when these impressions are not well understood they obviously leave no memories. The more importance one attributes to the localizing value of defects of memory in intracranial tumours the greater is one's disappointment in the end. One gains an impression that memory is much more a function of the brain as a whole rather than of any specific area. That defects of memory occasionally occur in prolonged increase of intracranial pressure, whatever the cause may be, is common knowledge. Probably patients with organic lesions of brain fail to fix or register an impression rather than forget a duly registered one. One can hardly speak of loss of memory in a patient who "forgets" the sensation of a pin-prick immediately after it is felt by him, as was the case in two patients of this series.

Changes in personality were observed in eight patients, or in 21 per cent., as contrasted with 50 per cent. in the series of frontal

lobe tumours. Since the appearance of these changes is usually insidious no reliable facts as regards the time of their development could be secured. However, a perusal of the records gives the impression that these changes appear at a considerably earlier date in frontal tumours than in tumours of the temporal lobe.

The changes in personality observed may be grouped under optimistic and pessimistic tendencies. In the first the patient appears from the beginning as unduly "sociable," loquacious and good spirited, and soon reaches a stage which is known as euphoric. He is cheerful and perfectly happy; he denies or minimizes his present symptoms, and there is often a persistent tendency to facetiousness. In the course of time his jokes become flat, dull and stupid; one patient would constantly seize on somebody's name and add something funny to it, as "Cecil—gristle," while another, when told to sit up, responded, "Sit up, good wife, and shake your feathers." It is interesting that even in a late stage of the disease, when the patient is hardly able to understand a simple command, he may still enjoy stupid catch-phrases of his own fabrication. This is so obvious and strange that it suggests to the observer that the entire mental energy of the patient is given over to this narrow and dull corner of intellectual life.

When changes in personality take a pessimistic shade, the most frequent state is one of depression. The patient is constantly worried over his condition; he becomes self-centred and extremely egoistic; nothing in the world matters if only he could be relieved of his trouble; he becomes irritable and suspicious; he is stubborn, and all suggestions from whatever source they come are met with distrust and suspicion; he suspects the faithfulness of his wife, and loses all interest in his family.

Both trends, the optimistic and pessimistic, finally lead to the condition known as "childishness," or, as the French authors call it, *puérilisme*. Childish interests in toys, plays, and stories, and a rapid transition from one emotional state to the other, as from crying to irresistible laughter and then again to weeping, is the mental state at which the patient arrives in the final stages of the disease.

The literature on prolonged sleep in intracranial tumours, or hypersomnia as Purves Stewart calls it, is very confused, and can be of little assistance in studying this symptom. The term "lethargy," which is used so frequently, is misleading, since lethargy includes not only true prolonged sleep or hypersomnia, but also the stupor which is a common symptom of prolonged severe increase of intracranial pressure. In the

present series hypersomnia was observed in 23 per cent. of all cases. In the tumours of the temporal lobe this symptom appeared on an average one month before admission to the hospital, and in most of these cases there was a history of actually prolonged sleep. In some it was described as extreme drowsiness, apart from headaches, with yawning and persistent nose rubbing. That nose rubbing is to be interpreted as a sign of sleepiness is suggested by observation of infants and small children. The prolonged sleep approximates to that of the symptomatic narcolepsies. It had been for long stated that tumours in the region of the third ventricle are often associated with pathological sleep, but a review of the nine cases of this series allows no definite conclusion on this question. In five cases, however, the lesion was basal and definitely involved the basal ganglia.

Mental confusion was seen in three cases only. One patient, an engineer by profession, persistently refused to believe that he was in a hospital; he was always "on my job." In a woman of 54, in whom mental confusion preceded the admission to the hospital by eight months, the first thing her daughter noticed was that "one morning she served breakfast on dinner plates." The third patient was completely disoriented in time and space, after an attack of severe headache and vomiting about two weeks before death.

Fits.—Although recognized by most authors, fits have not been given as much attention as they would seem to deserve as a symptom of tumours of the temporal lobe. The fact that the various epileptic equivalents which may be associated with these tumours are referred to throughout the literature by different and frequently misleading headings bears witness to it. To be of diagnostic significance a fit must indicate a local discharging lesion; it must have a local beginning, or at least it must allow a conclusion as to the lateralization of the lesion from the state of the reflexes and the condition of the patient immediately following it. It is mainly from this point of view that fits will be discussed below.

Fits of one kind or another were observed in nineteen patients of this series. That epilepsy is not a late symptom in all cases of temporal lobe tumour may be concluded from the fact that the first fit occurred on an average nine months before admission to hospital, the extremes being two weeks in a case of typical local motor seizures and four years in a patient with classical "dreamy states." Among the nineteen cases five had general epileptic seizures, but the onset in one of these cases was gradual enough to allow a lateralization of the discharging lesion, since

turning of the eyes and head to the opposite side always preceded the convulsions. In the other four cases the onset was too rapid and the condition of the reflexes immediately following the attacks too indefinite to allow a conclusion as to the seat of the lesion. Typical Jacksonian fits were observed in two patients; they first occurred late in the course of the disease, as one would expect from anatomical reasons, the average time being three weeks before admission to the hospital. In these two cases the fits commenced in the hand; although they localized the lesion they were of little diagnostic significance because of their late onset. Local sensory fits, including uncinate seizures, dreamy states, and visual and auditory sensations, are of far greater diagnostic importance.

Focal sensory fits occurred in twelve patients. The average length of time from the first fit to admission to the hospital was over ten months. In some of these twelve patients the fits consisted of combinations of various sensations. Uncinate seizures were seen in seven cases; in three of these they preceded dreamy states, with the more or less complete train of phenomena that accompany them. Dreamy states unpreceded by uncinate seizures occurred in four cases, and in one instance there was a definite auditory aura followed by a local motor fit. The uncinate seizures in one case were always ushered in by paræsthesiæ of the left foot; obviously such a combination at once localized the discharging lesion. In the other cases the uncinate fits, whether followed by dreamy states or not, had a purely localizing but not a lateralizing significance.

In neurology there have been few clinical discoveries that have remained stable and alive as long as Jackson's teaching on uncinate fits. The dreamy state is a most complex phenomenon which taxes greatly the self-analysing ability of the patient and the observing power and experience of the physician. Only persons with more than average intelligence are capable of observing and expressing in words their experiences during such a state; for the less intelligent it is too elusive, and the most one obtains in a history is a statement from the relatives that sudden attacks occur in which the patient appears "vacant with a lost look and mind." Of course, much depends upon the physician; forty years ago Jackson [8] pointed out that if the physician is waiting for a well-expressed dreamy state he will miss many a typical but slighter seizure. These facts suggest that dreamy states occur much more frequently, but remain unrecognized by the patient and physician.

Under the name of "intellectual aura" the dreamy state was long

known to occur in epilepsy. Jackson was opposed to this term because the dreamy state is not a warning but a striking symptom of a certain variety of epileptic attack. Though much has been written on this complex condition, Jackson's original description is probably the best of all. "This is a very elaborate or 'voluminous' mental state." Along with this mental state there is frequently a crude sensation of smell or taste, or an epigastric or other visceral sensation. Dreamy states are not always accompanied or preceded by uncinate fits, just as the latter are not constantly followed by dreamy states. There may be in the dreamy state loss of consciousness, or "over-consciousness" co-existing with a defect of consciousness to present surroundings. Such a co-existence of a defect of consciousness (to the present) with an "over-consciousness" (to reminiscences of the past) is not an exclusive feature of this variety of epileptic equivalent, and is in accord with phenomena observed in other epileptic variants. It is a well-established fact that a discharging lesion is accompanied not only by plus function but also by minus function; paralysis or paresis develops at the same time as the clonic movements.

For the description of a typical dreamy state I mention the history given by an intelligent female patient: "At first everything goes black: then I feel as though I am taken miles out of myself. I do not lose consciousness, but everything around me seems to recede into the distance. My family seems miles away; their voices sound as though they are talking miles off. There is a feeling of strangeness about everything, although you are in your own home. These attacks are accompanied by a taste in the throat and a smell in the nostrils like lysol. It is more like fumes coming up my throat." These attacks last about five minutes. They are preceded by "a feeling of warmth in the abdomen and a sensation as though everything inside were turned to boiling water." This sensation in the abdomen is so uncomfortable that she rubs the abdomen; as it passes off it is succeeded by the dreamy state. Immediately after an attack she belches a great deal of gas. Her relatives added that before an attack came on "her eyes looked vacant and bulged."

The dreamy states alone give no information as to the side of the lesion, but the visual hallucinations that may accompany them are of lateralizing importance when they occur in a part only of the visual field, as they are usually observed on the side contralateral to the tumour.

Visual hallucinations in organic lesions of the brain have formed a

most confused chapter in epilepsy. The widely-spread tendency of authors to group together without discrimination all visual sensations has continued for many years and is still occasionally met with in the literature in spite of a warning sounded by Jackson [8] forty years ago: "Before we can make good generalizations we must carefully analyse. To group together as 'visual warnings' colour projections, apparent alteration in the distance of external objects, and 'dreamy states' with definite scenes, is generalizing without previous analysis and is an attempt to organize confusion." For a proper evaluation of the clinical and pathological significance of visual phenomena it is imperative to distinguish crude visual sensations without definite outlines and vivid contents, from complex visual sensations—the true visual hallucinations. The general consensus of opinion to-day is that crude visual phenomena result from discharges spreading over the area striata of the occipital cortex. This discharge is projected to the corresponding point in the visual field and is perceived by the patient in the contralateral half of the binocular field of vision. In these cases the visual phenomenon is the dominating feature in the epileptic fit. On the other hand, complicated subjective visual sensations, the visual hallucinations proper, play only a subordinate rôle in the epileptic fit due to organic brain disease. They are never of the nature of an aura, but appear as one of the train of sensations following upon an uncinate seizure due to a discharging lesion in the region of the uncus. According to Jackson visual hallucinations are provoked by an irritating lesion in the region of the uncus. The interesting question why only an uncinate aura is capable of provoking complicated visual phenomena, while the visual sensations in the course of a visual aura are of a crude and primitive nature, must be left unsolved for the present. Phylogenetically the brain is an appendage of the organ of smell, the rhinencephalon being the oldest portion of the cerebrum; as Gordon Holmes [5] expresses it: "Even in man it (the rhinencephalon) may still serve as a storehouse of simple memories and associations."

Cushing [2] thinks that the visual hallucinations which occur with tumours of the temporal lobe bear some relation to the damage of the optic radiations, since in his cases the hallucinations were always referred to the side opposite that of the tumour, i.e., in the defective halves of the visual fields. In seventy-two cases of temporal lobe tumour from Cushing's clinic, Horrax [6] found visual hallucinations of a "more or less definite and complex nature" in twelve cases, and of a less definite character in five instances. Defects in the visual fields were present in

only five of the twelve cases at the time of the first appearance of the hallucinations. In one case the hallucinations preceded the first appearance of a small quadrantic defect by at least four months; in another case there was no visual defect at any time, and blindness prevented examination of the fields of vision in one patient. In the remaining four patients with visual hallucinations the states of the visual fields are not referred to. While the relationship between visual hallucinations and defects in the visual fields is inconstant, the associations of these hallucinations with uncinate fits or dreamy states was definitely established in "at least" (Horrax) thirteen cases out of the seventeen. These facts suggest strongly that the association of the hallucinations with defects in the visual fields is merely a coincidence.

What has been said of visual hallucinations also holds true for auditory hallucinations. In the opinion of Holmes [5], subjective auditory hallucinations are rare and less striking than other sensory phenomena. When an auditory aura begins independently of any other sensory phenomena the patient usually describes crude noises, or everything may appear silent. It is only when an auditory sensation follows an uncinate seizure that complex hallucinations, as of voices, occur. In my series an auditory aura was observed only once; a patient with a left-sided temporal lobe tumour heard on several occasions "horrible noises," which were followed by twitchings of the right foot and leg. The noises were referred to both ears equally. In a recent report [1] from Cushing's clinic, auditory hallucinations were described four times among ninety-nine temporal lobe tumours and six times among ninety-nine frontal lobe tumours. There was no reference in the report to the relations of these hallucinations to epileptic phenomena. The fact that these hallucinations were observed in six patients with frontal tumours, all of whom showed signs of psychosis, suggests strongly that these auditory hallucinations were psychogenic.

Motor and sensory disturbances.—It is obvious that in tumours of the temporal lobe motor and sensory disturbances are neighbourhood symptoms. This fact reduces their diagnostic importance, though they are frequently observed in the course of tumours of this lobe. In five instances of this series a lower facial weakness only was observed. In three other instances an isolated motor weakness of the upper extremity was seen. More extensive motor and sensory disturbances were more frequent. The entire side of the body, including the lower face, arm and leg, were affected in ten cases; in seven instances there was a combined paresis of the face and arm, in three others of the leg and

face, and in two the arm and leg were affected. The motor or sensory disturbances rarely amounted to paralysis or anæsthesia, and in the majority they were so slight as to require repeated examination before they could be regarded as definite symptoms. Their onset was insidious, but in one case a hemiparesis appeared suddenly and was probably due to a hæmorrhage into the tumour. Pure sensory disturbances were observed only in one instance, in which there was complete loss of postural sense on the contralateral side of the body. In two cases tactile hemihypæsthesia was accompanied by facial weakness of the same side. When the sensation of the face was impaired its asymmetry on movement was of no importance, since sensibility is as essential in mimicry as the function of the muscles.

A controversy exists in the literature as to the cause of the motor disturbances in tumours of the temporal lobe, whether the pyramidal tracts are involved in the cerebral peduncles, as Knapp maintains, in the internal capsule or in the motor cortex. The fact that in this series of tumours motor epilepsy occurred in seven cases only speaks for the rarity of involvement of the motor cortex. On the other hand, the frequency of facial weakness preceding the appearance of weakness of the upper extremity, or of both limbs, would suggest the cortical origin of the motor disturbances. The best example of the development of a hemiparesis of this nature was seen in a case with a right-sided tumour in which a left lower facial weakness was followed two months later by a weakness of the left arm, and three months later by weakness of the left lower extremity. While in the cortex the facial centre lies directly over the temporal pole, the topographical relations of the pyramidal fibres in the internal capsule are such that those to the facial nucleus remain far forward and cannot be involved before the fibres to the lower extremity are encroached upon by a tumour advancing from the temporal lobe. It is, therefore, natural to believe that when the motor weakness begins in the face and then extends towards the upper extremity it is a result of a cortical disturbance, but in cases where the weakness appears first in the lower extremity the lesion may be capsular. From anatomical reasons one would expect motor weakness of capsular origin to be combined with a hemianæsthesia and hemianopsia, but this was seen in one case only of the series, in a patient with a deep-seated tumour of the temporal lobe, in whom a slowly developing right hemiparesis was followed by a right hemihypæsthesia and a right homonymous hemianopsia.

Knapp lays much stress upon motor weakness produced by com-

pression of the cerebral peduncle. There were eight instances in this series where the cerebral peduncle or the pons was compressed by the tumour, especially by herniation of the temporal lobe through the incisura tentorii. A careful study of these cases gives little support to Knapp's contention, for in compression of the cerebral peduncle one would expect an involvement of the upper extremity first, but in the three cases with isolated motor weakness of the arm there was no pressure upon the peduncle. Apparently the compression of the peduncle or of the pons is extremely gradual and gives few, if any, physical signs on the neurological examination. In this respect it is of interest to mention three cases where the neurological findings were baffling until the post-mortem examination revealed the true situation. In a patient with a right-sided tumour, a definite weakness of the right side of the face was observed in the later stages of the disease. In another patient with a right-sided tumour the plantar response was definitely extensor on the right and flexor on the left side, and the right abdominal reflex was absent while the left was brisk. In a third patient with a left-sided temporal lobe tumour the left plantar response invariably remained an extensor while the right was a flexor, and the left abdominal reflex was absent but the right was present. A post-mortem revealed in all these three cases herniation of a portion of the involved temporal lobe through the incisura tentorii, with a resulting dislocation of the brain-stem to the opposite side and pressure of it against the edge of the tentorium.

A defect of conjugate deviation of the eyes deserves special attention. Gordon Holmes has repeatedly emphasized the diagnostic importance of defective conjugate deviation to the contralateral side in tumours of the frontal lobe; it is then a result of involvement, direct or through pressure, of the frontal ocular area in the region of the second frontal gyrus. In this series of tumours defect of conjugate deviation to the contralateral side was seen in six cases. In three of these the tumour was situated in and distended the temporal pole so that it pressed directly against the frontal lobe. In the other three cases the tumour lay deep in the temporal lobe and extended towards the base and the uncus. In two of these a large cyst was found directly beneath the superior temporal sulcus; in the third there was a diffuse large tumour. These observations are of interest, as Foerster [3] succeeded in provoking in man a contralateral conjugate deviation of the eyes by faradization in the region of the superior temporal gyrus.

Another motor symptom in this series was a homolateral, contra-

lateral or bilateral tremor of the extended extremities. When present it was especially well seen in the hands when the patient held them extended in front of him, with the palms facing down and the fingers slightly separated. The tremor was rapid, fine and vibratory, not unlike that seen in paralysis agitans, although of a smaller range and finer rhythm. It could often be best determined by holding one's palm against the separated fingers of the patient's outstretched hands. During muscular rest the tremor disappears. To observe the tremor one must examine the patient repeatedly, since occasionally it comes and goes. A similar tremor was first described by Grainger Stewart [20] in 1906 as a feature of tumours of the frontal lobe ; at that time Stewart said : "I have never met with similar tremor in association with tumours situated in other regions of the brain." The tremor described by Stewart is a homolateral phenomenon. In this series four cases had ipsilateral tremor, in seven patients the tremor was contralateral to the side of the tumour, and in three it was bilateral but much slower and coarser in the contralateral hand than in the ipsilateral, and suggested the unsteadiness which one observes not infrequently in asthenic patients. The rapid fine vibratory tremor on the other side resembled that seen in exophthalmic goitre.

Attempts have been made to determine the anatomical and physiological basis of this tremor. The most probable explanation is that of Schwab [19], who regards it as part of a pallidum syndrome, basing his conclusion on six cases of temporal lobe tumour, in three of which a complete pathological examination was possible. According to him the tumour, by pressing upon or invading the putamen, releases the globus pallidus and consequently the pallidum syndrome, including the tremor, results. From this hypothesis one would expect tremor of the contralateral hand, while in my series it was seen in the ipsilateral or contralateral hand, and even bilaterally. It is of interest that neither the putamen nor globus pallidus was involved directly or by pressure in any of the cases with contralateral tremor, while in two of the cases with a homolateral tremor the corpus striatum was involved. There were, however, eight other cases with extensive involvement of the lenticular nucleus in which no tremor was seen.

The contention of some authors that the tremor is due to involvement of the thalamus is untenable, since it is impossible for a temporal lobe tumour to invade the thalamus without encroaching on the lenticular nucleus and internal capsule. The fact that the tremor was seen in some cases in the ipsilateral hand, in some in the contra-

lateral, and in some bilaterally, makes it difficult to explain it by any one hypothesis. My discussion of this symptom is only destructive, but if it is of any diagnostic significance in tumours of the temporal lobe it certainly is not of lateralizing value as Schwab suggested.

Reflexes.—Changes in the deep or tendon reflexes are of little diagnostic importance in temporal lobe tumours, since by the time they are demonstrable the tumour is in an advanced stage and most probably can be localized by some other symptoms. Following the general rule in cases with prolonged increase of intracranial pressure due to intracranial tumour, the patellar reflexes disappear much earlier than the Achilles jerks, while in meningitis the Achilles jerks are abolished first.

The abdominal reflexes are of more diagnostic value, and especially the upper or epigastric reflexes. A difference in the reflexes of the two sides is more important than the presence or absence of the reflexes on both sides. Frequently the only change is a slower response and quicker tiring out of the response on the side contralateral to the tumour. In this series the abdominal reflexes were present and equal on both sides in thirteen cases, and in eight instances they were absent on both sides; they often disappear completely when the patient's condition becomes grave. In fifteen patients the contralateral abdominal reflex was completely absent, or slower in response, and tired out more quickly than that on the ipsilateral side. In thirteen cases this condition was found on admission of the patients to hospital, and only in two did the normal reflex disappear during the patient's stay in hospital. In two cases the abdominal reflexes were absent on the ipsilateral side; these were the cases in which the contralateral side of the brain-stem was pressed against the incisura tentorii.

The plantar reflex is of less diagnostic importance. In temporal lobe tumours an extensor response appears as a rule somewhat later than the disappearance of the abdominal reflex. The typical extensor reflex is a slow, meditating response as though the peripheral irritation has to travel up the cord and back to the toes, but turning of the foot inward, with raising of the knee, and slight fanning of the toes frequently precede this typical extensor response. In my series the state of the plantar reflexes was definitely recorded in thirty-four cases. In thirteen there were normal flexor responses (one right and twelve left-sided tumours); bilateral extensor responses were obtained in three patients (one right- and two left-sided tumours); contralateral extensor responses were present in nine patients (all right-sided tumours); in eight

instances (four right- and four left-sided tumours) the contralateral reflex was a doubtful extensor. Not infrequently a plantar response remains questionable or difficult to elicit for several days before becoming typically extensor; this is especially true during bouts of severe headaches and vomiting. Reference has been made to the fact that the plantar as well as the abdominal reflexes may become decisive in the lateralization of the tumour immediately after a generalized epileptic convulsion.

Disturbances in gait and balance.—Considerable attention has been paid in European literature to disturbances of gait and balance in tumours of the temporal lobe. According to Knapp and others, such disturbances are frequent, and with past-pointing and nystagmus form the so-called "pseudocerebellar symptom-complex" of temporal lobe tumours. These symptoms have been explained by different hypotheses. The oldest explanation was that the temporal tumour pressed upon the cerebellum through the tentorium, but it has at present few adherents, as only an enormous pressure could be effectively transmitted through the tense and inelastic tentorium, and then it would probably not affect one cerebellar hemisphere only. Knapp has suggested the presence in the temporal lobe of a mechanism which presides over the balance of the body in the same way as the cerebellum does, and according to him it is a disturbance of this mechanism that disturbs gait and balance. Working upon this hypothesis he refers to these symptoms as "temporal lobe ataxia." Recently Schwab [19] attempted to explain this ataxia by involvement of the temporo-pontine and temporo-thalamic fibres which are connected with the opposite side of the cerebellum.

In this series of cases a cerebellar type of gait was seen only once. In one patient with a left-sided temporal lobe tumour there was invariable pastpointing with the left hand outwards, while the right pointed correctly. This single case of error in pastpointing speaks against Schwab's contention that in tumours of the temporal lobe the contralateral hand deviates inwards in the finger to nose test, so that the finger, so to say, points towards the position of the tumour.

In five cases spontaneous nystagmus was observed, ipsilateral nystagmus was present in three right-sided tumours, a contralateral nystagmus in one right-sided tumour and a rotatory nystagmus in another right-sided tumour. None of the left-sided tumours showed nystagmus.

Thus the incidence of cerebellar symptoms and signs was exceedingly small in this series of cases. It is true that many patients were bed-

ridden even on admission to the hospital, so that an examination of the gait was not possible, but the scarcity of other cerebellar signs speaks against the diagnostic importance given them by European authors.

Visual disturbances.—Since Cushing [2] in 1921 drew attention to the importance of visual disturbances in the diagnosis of tumours of the temporal lobe, this symptom has been looked upon by many as an almost *conditio sine qua non* of lesions of this region of the brain. The influence of Cushing among neurological surgeons and American neurologists, and the persuasive clarity of his writings, have much contributed to this. Being primarily interested in the localizing significance of partial defects in the fields of vision in tumours of the temporal lobe, he concluded from a detailed study of his cases that a lesion here may produce homonymous defects in the upper or lower quadrants, while lesions posterior to the temporal lobe are more likely to cause a complete vertical homonymous hemianopsia. From among 59 tumours of the temporal lobe he selected 39 cases in which "the perimetric findings were reliable." In 6 of these 39 cases no field defects of any kind were found, in other words, in 26 cases out of 59, or in 45 per cent. of all the temporal lobe tumours of his series the perimeter proved futile as an aid in diagnosis. In the remaining 33 cases there were visual field defects definite enough to indicate the side of the lesion. A symptom so valuable and frequent is, of course, of great importance in the localization of lesions in what is, *par excellence*, a silent brain area. In the present series of 38 temporal lobe tumours, this symptom was present much less frequently than in Cushing's material. This is of especial interest as in the series of nine tumours of the temporal lobe studied in 1911 by Kennedy [9], while connected with the National Hospital, no defects in the fields of vision were present.

Of the 38 cases of this series examination of the visual fields was reliable in only 28 cases, or in about 74 per cent. as compared with 66 per cent. of Cushing's series. Of these 28 cases a concentric constriction was present in three cases and no visual field defect was detected in thirteen instances. Homonymous visual defects which helped to lateralize the tumour were present in only seven cases: in one instance there was a partial upper quadrantic loss, in the other six there were defects of the temporal sickle more or less approaching the classical midline hemianopsia. Of course, one could argue that these extensive defects in the visual fields show that our cases were far advanced, but if so why is a complete hemianopsia not more often met with? That Cushing's cases were not all in an early stage is obvious

from the fact that in twenty out of fifty-nine "cerebral convulsions" (Cushing) were a definite symptom. To assume that hemichromanopsia was present in our patients but not discovered in the usual perimetric examination with white discs is hardly possible, since the patients were usually kept in the hospital long enough for the development of defects to white. It is generally conceded to-day that quantitative perimetry is more reliable than the qualitative or colour perimetry, as the loss of visual perception increases first of all with the decrease in size of the test object, and only in the second place does it depend upon the colour of that object.

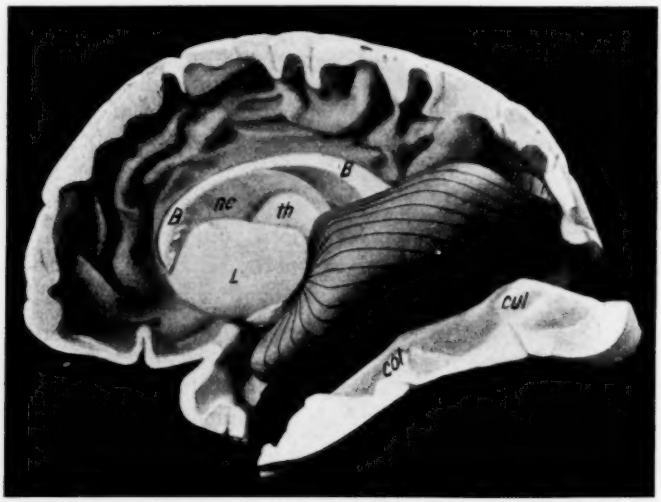

FIG. 1.—The course of the optic radiation, showing the relation of the fibres to the inferior and the posterior horns of the lateral ventricle, and to the cortex of the temporal and occipital lobes. *K*, the temporal knee of the radiation; *B*, corpus callosum; *L*, nucleus lenticularis; *nc*, nucleus caudatus; *th*, thalamus opticus.

A portion of the temporal and occipital lobes is slightly displaced downwards to show the relation to the optic fibres of the gray matter in the region of the fissura collateralis (*col*); *cul* marks the highest point of this invagination of the cortical gray matter. (From Pfeifer.)

As the optic radiations pass through the temporal lobe one naturally would expect defects in the visual fields in most temporal tumours. Certain anatomical considerations, however, suggest an explanation of the actual clinical facts. Whatever may be the position of the optic radiations in the stratum sagittale externum, the stratum sagittale internum and the tapetum, they certainly pass around the walls of the inferior and posterior horns of the lateral ventricle. In the posterior half of the

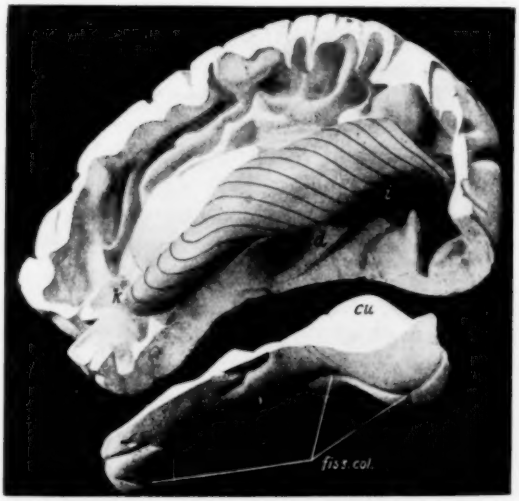

FIG. 2.—The optic radiation viewed from the lateral, anterior and inferior aspects, showing the ventral bundle of the radiation winding about the inferior horn of the lateral ventricle, as it passes towards the oral portion of the area striata. *k*, temporal knee; *fiss. col.*, fissura collateralis. (From Pfeifer.)

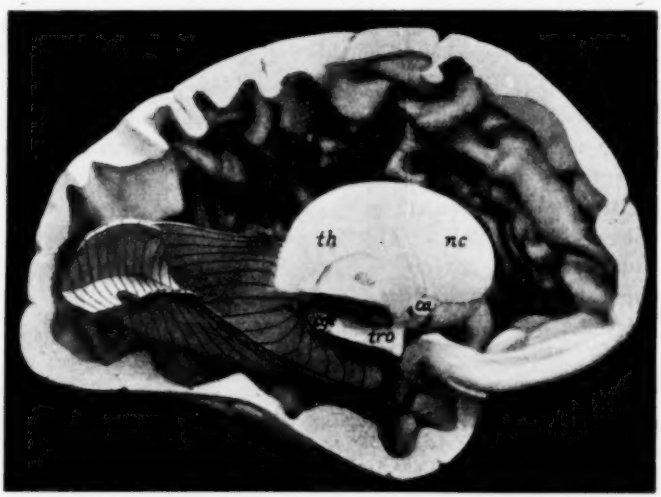

FIG. 3.—The optic radiation in a left cerebral hemisphere of which only the cortex is left. The mesial part of the cortex has been removed also. *th*, thalamus opticus; *nc*, nucleus caudatus; *ca*, commissura anterior; *ci*, capsula interna; *cgi*, corpus genicul. int.; *cge*, corpus genicul. ext.; *tro*, tractus opticus. (From Pfeifer.)

temporal lobe the optic fibres are closer to the gray matter of the convolutions than in its anterior part, and, consequently, tumours arising in or extending to the posterior half of the lobe are more apt to cause a homonymous defect in the fields than growths in the anterior half. In four of the six cases of this series with visual defects approaching complete hemianopsia, the tumours were situated in the posterior half of the lobe, and in the other two they extended sufficiently deep to involve the whole optic radiation as it leaves the internal capsule; in these two cases the visual defects were associated with hemihypæsthesia. The fibres of the visual pathway are less vulnerable as they wind around the ventricular wall than where they lie in a less elastic and yielding neighbourhood, since the wall of the ventricle is displaced slowly by the gradually increasing pressure from the tumour, and the optic radiations following it may preserve their function for a time. In one of the seven cases hemianopsia was an intermittent symptom, appearing when headaches were most severe, and disappearing when they grew less. This is probably due to intermittent distension of the ventricle by sudden changes in the circulation of the cerebro-spinal fluid, and also possibly to œdema about the tumour. Only diffusely growing tumours, which destroy and replace, rather than displace, the surrounding tissues, involve the optic fibres early.

The ventral bundle is the most vulnerable part of the optic radiations. After leaving the internal capsule, this bundle runs forward, downward, and outward, in the direction of the temporal pole; it then turns sharply around the inferior horn of the lateral ventricle, forming the temporal knee of the visual path, and runs backward close to the inferior and infero-lateral wall of the inferior horn. It is this portion of the visual radiation that supplies the upper lip of the fissura calcarina, and according to Fleischer and Pfeifer [17] it contains the fibres for the temporal sickle of the field. The topographical relations of the optic radiation in the temporal lobe may be visualized from the illustrations (figs. 1, 2, and 3), taken from Pfeifer's monograph on the anatomy of the visual path. In an ingenious way Pfeifer reconstructed the optic radiation from serial sections of the brain, and in this manner studied their relations to the cortex. It is easy to see what a large part of the temporal lobe contains no visual fibres, and in this area a tumour will naturally cause no visual disturbances of localizing value.

A contralateral inattention hemianopsia, when tested in the routine way customary at the National Hospital, was observed in five cases among the twenty-eight in which the visual fields were reliably examined.

That a rough test for visual inattention is more sensitive than a perimetric examination, however expert the examiner may be, is seen from the fact that in not one of these five cases did repeated perimetric examination reveal any visual defect.

In evaluating these observations, it must be remembered that, according to psychologists, visual attention on the right side is normally greater than that on the left. The five cases (two right-sided and three left-sided tumours) with the visual inattention but negative perimetric findings, added to the sixteen cases with normal visual fields, give a total of twenty-one cases where perimetric examination was of no actual help in lateralizing the lesion. In other words, in a series of thirty-eight cases of temporal tumour, the perimeter was valuable in the diagnosis in only seven instances, or in 18·5 per cent. This result makes one doubt the validity of Cushing's statement that "the perimeter as a diagnostic aid in temporal lobe tumours is possibly the most important agent of all."

Subjective visual disturbances were of no localizing significance. There were complaints of visual disorders in eighteen cases. The most frequent symptom was failing vision, which was present in fifteen patients, and commenced on the average 3·5 months before admission to the hospital. Three patients complained of transitory momentary amblyopia, which is probably a result of rapidly progressing papillœdema. Post-mortem findings in these three patients gave no support to the opinion expressed in the literature that such a transitory amblyopia in intracranial tumours is a result of a periodical distension of the third ventricle with fluid.

Hearing.—Notwithstanding the generally accepted view that the cochlear fibres of the auditory nerves do not decussate completely, and that each auditory nerve is connected with both hemispheres, from time to time reports appear in the literature of complete deafness in the ear contralateral to the side of a temporal lobe tumour. That partial loss of hearing may accompany temporal tumours is suggested by reading carefully taken histories of such patients. Little is known of partial disturbances of hearing, because of the inadequacy of present-day methods of testing it. In this series of cases there were definite disturbances of hearing, though the ears were normal, in three patients. One with a left-sided temporal lobe tumour noticed increasing deafness in the left ear for a year before admission to the hospital, and this actually was his first symptom. Another patient with a left-sided temporal lobe tumour was so deaf that he could not understand simple

questions, but this was partly due to aphasia. A third patient, with a right-sided temporal lobe tumour, gradually lost hearing in both ears about two months before admission to hospital. It is interesting that the patient with the auditory sensory auræ and local motor fits had no disturbance of hearing. Three instances only, in a series of thirty-eight cases, cannot justify definite conclusions, but I believe that progressive failure of hearing in both ears, in a patient with an intracranial tumour, should, in the presence of normal cochleæ, put one on the look-out for a temporal lesion.

Disturbances of smell and taste.—The present-day methods of testing of smell and taste lack the preciseness and the objective character of the examination of vision. Most likely it is due to the defects in our tests that disturbances of smell and taste are rarely observed in temporal tumours in the intervals between epileptic fits, notwithstanding the fact that the olfactory centre is situated in the temporal lobe. Complete anosmia and ageusia hardly ever occur in uncomplicated cases. It is only when the tumour extends forward along the orbital roof and involves the olfactory tract that it causes complete anosmia.

In my series disturbances of smell and taste were observed in three patients. One patient with a right-sided tumour had a bilateral defect of smell and impaired taste. In another patient with a right-sided tumour perseveration of smell and taste on both sides was observed. In a third patient with a left-sided tumour taste was completely absent on the entire left side of the tongue, though the trigeminal and the facial nerves were apparently not involved. All the three patients were ignorant of these disturbances before examination. I have repeatedly seen in intracranial tumours, not only in those situated in the temporal lobe, a slight depression of the acuity of smell and taste, which is merely a result of increased intracranial pressure. Authors who describe disturbances of smell as a homolateral symptom and disturbances of taste as a contralateral symptom of tumours of the temporal lobe are greatly in advance of the position suggested by a study of clinical material.

Disturbances of speech.—The differentiation into different groups of disturbances of speech according to the degree of involvement of the various components of normal speech is of doubtful value in the symptomatology of temporal tumours. The type of the tumour, its position and size, the condition of the ventricular system, and finally the reaction of the surrounding brain tissue, are all factors in determining varying defects of speech. It is obvious that attempts to localize precisely a tumour from the nature of the speech disturbances it has

produced are full of pitfalls. There is probably more truth than error in Cushing's statement that the aphasia associated with temporal lobe tumours is a neighbourhood rather than a focal symptom. As a rule, however, the disturbances of speech produced in the early stages by tumours of the temporal lobe are of the usual types, and the most frequent symptoms are loss of power to recall words and to name objects, places and persons.

Aphasia was observed in twelve of the twenty-one cases of left-sided temporal tumour, excluding one case in a left-handed person. The disturbances of speech set in on an average five weeks before the admission of the patient to hospital, but in four cases only aphasia was the first localizing symptom. The most striking feature in one patient was inability to understand spoken or written words, and to write. In three other patients there was only a difficulty in naming objects, places and persons. In the remaining eight patients the disturbances of speech were complex. In these the first symptom was usually the occasional want of words in conversation, and then the use of wrong words, the difficulty increasing until the patient talks only jargon, his words are all "jumbled up," as the wife of one patient expressed it, he utters strings of words without meaning, and many words are of his own fabrication, frequently he is not aware of his errors. This verbal aphasia is, however, preceded by a nominal aphasia; the patient cannot recall the names of objects and persons, although later the name may come into his mind quite readily. In three cases the patient could not read, in two they were unable to write, and in two others there was definite evidence of apraxia. Defects of articulation were completely absent in all these cases.

The fact that aphasia was the most important localizing sign in only four cases out of twenty-one left temporal lobe tumours, and was present in twelve cases only, indicates that it is not, as it has been considered for long, the most prominent symptom in left-sided tumours. An analysis of the cases in which speech was normal shows that aphasia does not occur in basal temporal tumours, and that small tumours may invade the temporal lobe without disturbing it.

Much has been written on those rare cases in which aphasia accompanied a tumour of the right temporal lobe in a right-handed patient. This series includes no such case. I believe that in such cases the aphasia is due to compression against the skull of the dislocated left hemisphere, rather than to the presence of a speech centre in the right temporal lobe. I have seen a case in which left unilateral hydrocephalus

associated with a right-sided cerebral tumour produced aphasic symptoms.

Cranial nerves.—Only the first five cranial nerves come into consideration in connection with tumours of the temporal lobe. The optic and olfactory nerves have been dealt with above. Among the other four cranial nerves, the oculomotor and the trigeminus occupy the most prominent place. The topographical relations of these nerves to the temporal lobe are so intimate that it is not surprising that they often furnish important localizing signs. It is true, however, that the tumour may compress the oculomotor nerve without producing clinical signs, probably owing to the nerve being displaced gradually.

In a paper to which I have already referred, Kennedy says: "In none of these cases (nine temporal lobe tumours) was this result (partial third nerve paralysis) observed, nor was it present in the other cases of temporal tumour which have come under my observation." This statement is perplexing in view of the evidence to the contrary presented by Knapp and others. Almost forty years ago, MacEwen [12] first called attention to paresis of the third nerve in association with temporal tumours. About twenty years later, Knapp attempted to classify the various oculomotor paretic signs observed in these tumours, and since then he has repeatedly emphasized the importance of partial third nerve paralysis. While an analysis of the findings in the present series of cases confirms in the main the diagnostic significance of partial third nerve paralysis in temporal lobe tumours, I doubt the validity of Knapp's explanation of its pathogenesis.

Oculomotor palsies were observed at one time or another during the patients' stay at the hospital in twenty-one patients. Contrary to Knapp's frequently stressed statement that ptosis is the most frequent symptom, in these twenty-one cases it was observed in seven instances only, while pupillary changes were present in eighteen patients. Ptosis was observed on the ipsilateral side in four patients, in one it was contralateral and in two bilateral. The pupillary changes and the ptosis are transitory but recurring phenomena, and become persistent late in the disease.

There may be changes in the size of the pupil and in its shape; the former are more common, as in seventeen instances there were alterations in the size of the pupils and in only four changes in shape, and in three of these it accompanied changes in size.

In his studies of the symptomatology of temporal tumours, Knapp always speaks of mydriasis of the ipsilateral pupil as the most prominent

change, but a study of my material does not bear this out. Continuous observation of a patient with a temporal tumour may show at first an extremely slight myosis of the ipsilateral pupil which may be so slight that it requires repeated examination; it may remain for a day or two and then disappear, to return later in more marked degree. Finally, it becomes persistent and well marked, but as the tumour grows the pupil becomes dilated and much larger than its normal fellow, myosis gives way to mydriasis. This state persists up to the end if the disease is left to its natural course. These changes in the size of the pupil were actually followed in six patients of this series. In the others operation was undertaken before myosis gave way to mydriasis.

The fact that mydriasis appears only towards the end, and that ipsilateral myosis is the leading pupillary change in temporal tumours, has an anatomical explanation much less hypothetical than those offered by Knapp and by Mingazzini. Knapp maintains that ptosis always precedes the pupillary changes, and to explain it assumes that the fibres for the levator palpebræ are more vulnerable than the other fibres of the oculomotor nerve, and, therefore, in a slight affection of the nerve they suffer first. Mingazzini's suggestion [13] that the ptosis is of cortical origin and occurs when the superior temporal gyrus is involved is entirely at variance with all clinical and pathological evidence.

The fact that myosis and ptosis are the only signs of oculomotor paresis and that weakness of the external ocular muscles is absent until late in the disease, and even then is extremely rare, at once suggests that they are not due to lesions of the oculomotor nerve itself. Myosis and ptosis are the most obvious components of the so-called Horner's syndrome, which is produced by a lesion of the sympathetic fibres to the head. The oculopupillary sympathetic fibres reach the base of the brain as the plexus caroticus internus along with the internal carotid arteries. There the plexus divides into two bundles; one accompanies the oculomotor nerve and the other runs to the Gasserian ganglion and joins the first division of the trigeminus. The latter fibres pass to the eye in the company of the ciliary nerves (naso-ciliary and long ciliary) and supply the dilator pupillæ; the fibres accompanying the oculomotor supply the involuntary palpebral muscles. For anatomical reasons the first division of the fifth nerve, before it disappears in the foramen rotundum, is especially liable to pressure by an enlarged temporal lobe and the sympathetic fibres loosely attached to it are the most liable to suffer from such pressure. At first this produces a paresis of the dilator

pupillæ and myosis of the ipsilateral pupil, which is transitory, since the pressure provoking it varies with the periodic disturbances of the circulation of the cerebrospinal fluid and of intracranial pressure. When the sympathetic fibres accompanying the third nerve are compressed, the involuntary palpebral muscles relax and ptosis ensues.

In my series ptosis was less frequent than myosis, and made its appearance at a relatively later date. This is readily explained by the fact that the oculomotor nerve, which is accompanied by the palpebral sympathetic nerve fibres, is less firmly fixed in its intracranial course than the first division of the trigeminus, and, therefore, responds to pressure later. On the further enlargement of the temporal lobe in the later stages of the disease, the oculomotor and the trigeminal trunks are involved by the increasing local pressure; then the sphincter pupillæ is paralysed and ipsilateral mydriasis replaces myosis.

I consequently regard the early oculopupillary changes in temporal tumours as part of an incomplete Horner's syndrome. Enophthalmos is less frequently observed, especially as it is apt to be transitory. The instillation of cocaine in the eye to determine whether the pupillary changes are due to a paresis of the third nerve or to a paresis of the oculopupillary sympathetic fibres, would be of diagnostic interest, but it was not carried out in any case of the present series.

The fact that, notwithstanding the relative frequency of herniation of a portion of the temporal lobe through the incisura tentorii and the pressure frequently exerted by the enlarged temporal lobe on the interpeduncular space, complete third nerve palsies are not seen in these cases, still further supports the explanation that the oculo-pupillary changes are due to involvement of the sympathetic fibres and not of the oculomotor. In only two cases of this series was a paresis of the internal rectus observed, and in both it appeared simultaneously with mydriasis. In these two cases no herniation of the temporal lobe through the incisura tentorii was found. On the other hand, there was no evidence of paresis of the oculomotor nerve, and a sympathetic homolateral myosis in only one, of the three cases in which pressure of the cerebral preduncles against the edge of the incisura tentorii caused a homolateral lower facial weakness, absence of the homolateral abdominal reflex, or a homolateral extensor plantar response.

It is generally admitted that absence of the corneal reflex is a most delicate index of involvement of the first branch of the trigeminus, but it is of value only in those cases where there is no hemiparesis or hemihypæsthesia of the same side. After excluding all cases of corneal

areflexia in patients with central motor or sensory disturbances there remain seven cases in which the ipsilateral reflex was diminished or lost. In one of these, in a patient with a contralateral central hemihypæsthesia, the corneal reflex was absent on both sides.

Sir William Gowers [4] has pointed out the fallacy of relying, in advanced intracranial tumours, upon an abducens paralysis as a localizing sign. As far as I am aware, the literature of temporal tumours contains only a single case, that recorded by Knapp, with a bilateral paralysis of the abducens. Knapp has repeatedly stated that paresis of the abducens nerve is very rare in temporal tumours. In at least seven cases of this series the sixth nerve was involved; in three the external rectus muscle was merely weak, in the other four it was completely paralysed. These disturbances were present when the patients were admitted to hospital. In five patients the paresis was unilateral, in the other two it was bilateral. When unilateral it was always on the side of the tumour. In the bilateral cases the external rectus muscle on the side of the tumour was completely paralysed, while the opposite muscle was only weak. The frequency of involvement of the abducens nerve in temporal lobe tumours would be even greater if the transient diplopia of which four other patients complained—though there was no demonstrable ocular palsy—could be attributed to a temporary weakness of an external rectus muscle.

Summary and Conclusions.

The main criticism that may be advanced on the conclusions drawn by individual writers on the symptomatology of tumours of the temporal lobe is that they attempt to establish too rigid and too definite symptom-complexes. The temporo-sphenoidal lobe is too large an area of brain for it to be possible for lesions of it, variable in type and extent, to produce any one definite train of symptoms and signs. For these reasons I shall not attempt to formulate here a definite temporal lobe syndrome, but shall merely enumerate the various symptoms and signs in the order of their frequency in this series of thirty-eight tumours of this lobe.

Headaches.—Although complained of by every patient in this series, headaches *per se* are of no localizing value. Local pain or tenderness, which was observed in ten patients (26 per cent.), is of greater value. It is frequently quite characteristic; it is a sharp, agonizing pain, comes on suddenly in paroxysms and disappears abruptly. It is probably due to local pressure on the branches of the trigeminal nerve.

Vomiting was present in 50 per cent. of the cases. It has no localizing significance and, as in other intracranial tumours, is merely a symptom of increased intracranial pressure.

Papillœdema.—Definite œdematous changes were seen in the optic discs in 86 per cent. of the cases. The comparative degree of swelling of the nerve heads on the two sides is of lateralizing value only in the incipient stages of the papillœdema.

Incontinence.—This symptom was present only in 20 per cent. of the cases. While in frontal lobe tumours sphincter disturbances seem to be a result of psychic disorders, in temporal growths they are merely a symptom of increased intracranial pressure.

Psychic disturbances.—The diagnosis of an intracranial tumour cannot possibly be made from the presence of psychic disturbances alone; however, when the diagnosis has been made from other symptoms and signs, certain psychic disturbances may help to localize the tumour in one or another part of the brain. Defects of memory were present in 50 per cent. of the cases of this series; a disturbance of memory was observed in a nearly equal proportion of frontal tumours, but it is not unusual in tumours of the temporal lobe to observe a loss of memory for both recent and past events, while in tumours of the frontal lobe it is only the recent events that are not remembered by the patient. Changes in personality, hypersomnia, and mental confusion are of little value in distinguishing between temporal and frontal tumours; they are, however, of some importance when subtentorial tumours are to be considered, for with these they hardly ever occur. The tendency to attribute psychic disturbances to lesions of the left hemisphere in right-handed people is not supported by clinical facts, and, therefore, they have no lateralizing value.

Fits.—Fits occurred in 50 per cent. of the cases, but only in 40 per cent. were they of localizing or lateralizing value. They were a relatively early symptom, especially focal sensory fits, which were observed in 32 per cent. of the cases. Uncinate fits and dreamy states are of merely localizing value, but the visual hallucinations that may accompany them are of lateralizing importance when they occur in a part only of the visual field. The visual sensations which occasionally follow closely on the uncinate auræ are of a complex nature, and thus differ from the crude visual phenomena occurring in fits associated with lesions of the occipital cortex.

Motor and sensory disturbances.—Although obviously a neighbourhood symptom, motor and sensory disturbances were observed in 92 per

cent. of the cases of tumours of the temporal lobe. In twelve patients the whole contralateral side of the body was affected; in seven there was weakness of the arm and face only; in five a weakness of the face alone was seen; in three the contralateral arm alone was involved; weakness of the leg and face was present in three instances, and in two patients there was paresis of the arm and leg. A defect of conjugate deviation of both eyes to the contralateral side was present in six patients. In fourteen patients a fine vibratory tremor of the hand was observed, in the ipsilateral hand in five cases, in the contralateral in seven cases, and in the remaining three it was bilateral. The most constant of the motor and sensory symptoms was a contralateral lower facial weakness; it was observed in 66 per cent. of all the cases of this series. The abdominal reflex is not so important as a lateralizing sign; only in fifteen patients (39 per cent.) was it decisive on this point. A definite contralateral extensor plantar response was seen in nine patients, and in eight the response was a doubtful extensor; in other words, the plantar response had a lateralizing value in about 45 per cent. of all cases. In general, the extensor plantar response is a somewhat later sign than the disappearance of the abdominal reflex.

Disturbance of gait and balance.—The findings of this series of cases give no support to the hypothesis of the existence in the temporal lobe of an organ of balance. The so-called "pseudo-cerebellar signs" are rarely seen in temporal lobe tumours, and even when present are of no localizing or lateralizing significance.

Visual disturbances.—The mere fact that trustworthy examinations of the visual fields were possible in 74 per cent. only of the cases of this series detracts from the diagnostic importance of visual disturbances in tumours of the temporal lobe. Defects of lateralizing importance were found in only seven cases (18 per cent.). In over 46 per cent. of the twenty-eight cases with reliable examinations the fields were normal. The relative rarity of defects in the visual fields in tumours of the temporal lobe is explained by the fact that the fibres of the optic radiations, in their course towards the area striata, wind around elastic and yielding structures, the inferior and the posterior horns of the lateral ventricle.

Disturbances of hearing have little localizing and no lateralizing value, but increasing impairment of hearing in both ears in a patient with an intracranial tumour should suggest a temporal lesion, provided, of course, that the cochleæ are normal.

Disturbances of smell and taste are of no localizing or lateralizing value in tumours of the temporal lobe.

Speech disturbances.—It is obvious that disturbances of speech when present in a right-handed person assist greatly in the local diagnosis. That aphasia is not of as great diagnostic importance as one is led to believe from the literature is evident from the fact that in twenty-one right-handed patients aphasia was a definite symptom in twelve cases (57 per cent.) only, and was the first localizing sign in only four patients.

Cranial nerves.—Oculo-pupillary changes were observed in twenty-one patients (55 per cent.); eighteen of these showed pupillary changes, either myosis or mydriasis, and ptosis was present in seven patients. The oculo-pupillary changes are transitory, and recur from time to time, but become permanent late in the disease. The commonest change is in the size of the pupil; changes of shape were seen only four times. An early slight transitory recurrent ipsilateral myosis is a relatively frequent sign. It is due to involvement of the sympathetic fibres accompanying the first division of the trigeminus which innervate the dilator pupillæ. At about the same time the sympathetic fibres accompanying the oculo-motor and supplying the involuntary palpebral muscles may be involved and ptosis result. Later in the disease, when the constantly increasing pressure of the enlarged temporal lobe leads to compression of the oculo-motor trunk proper, the sphincter pupillæ becomes paralysed and myosis gives way to mydriasis. In the same way further pressure on the first division of the trigeminus may produce ipsilateral loss of the corneal reflex.

Notwithstanding the relative frequency of herniation of a portion of of the temporal lobe through the incisura tentorii, and of the pressure exerted by the enlarged temporal lobe on the interpeduncular space, complete oculomotor paralysis is not seen in these tumours.

An involvement of the ipsilateral abducens was present in seven cases. In two of these cases the paresis was bilateral, but only the ipsilateral nerve was completely paralysed.

It is my pleasant duty to acknowledge my indebtedness to the members of the staff of the National Hospital, Queen Square, London, for their permission to make use of the material on which this contribution is based, and to express my thanks to Dr. Gordon Holmes for criticisms and suggestions.

LITERATURE.

[1] COURVILLE, C. B. "Auditory Hallucinations provoked by Intracranial Tumours," *Journ. Nerv. and Ment. Dis.*, 1928, **58**, 265.

[2] CUSHING, HARVEY. "The Field Defects produced by Temporal Lobe Lesions," *Brain*, 1921, **44**, 341.

[3] FOERSTER, OTFRIED. Quoted by Schwab, in "Zur Diagnose der Schläfenlappentumoren," *Deutsch. Zeitschr. f. Nervenheilk.*, 1925, **84**, 42.

[4] GOWERS, Sir WILLIAM. "Diseases of the Nervous System," 1893, **2**, 180.

[5] HOLMES, GORDON. "Local Epilepsy," *Lancet*, 1927, **2**, 957.

[6] HORRAX, GILBERT. "Visual Hallucinations as a Cerebral Localizing Phenomenon, with Especial Reference to their Occurrence in Tumours of Temporal Lobes," *Arch. Neurol. and Psychiat.*, 1923, **10**, 532.

[7] HORSLEY, Sir VICTOR. In a discussion of a paper by Paton on "Optic Neuritis in Cerebral Tumours," *Trans. Ophth. Soc. U. Kingdom*, 1908, **28**, 136.

[8] JACKSON, HUGHLINGS. "On a Particular Variety of Epilepsy ('Intellectual Aura'), &c.," *Brain*, 1888-1889, **11**, 179.

[9] KENNEDY, FOSTER. "The Symptomatology of Temporo-Sphenoidal Tumours," *Arch. Intern. Med.*, 1911, **8**, 317.

[10] KNAPP, ALBERT. "Die Tumoren des Schläfenlappens," *Zeitschr. f. d. g. Neurol. u. Psychiat.*, 1918, **42**, 226.

[11] *Idem.* "Die Geschwülste des rechten und linken Schläfenlappens." Wiesbaden: J. F. Bergmann, 1905.

[12] MACEWEN, WILLIAM. "The Surgery of the Brain and Spinal Cord," *Brit. Med. Journ.*, 1888, **2**, 307.

[13] MINGAZZINI, G. "Sui tumori del lobo temporale sinistro e dell' angolo pontocerebellare," *Riv. di Patol. nerv. e ment.*, 1911, **16**, 457.

[14] NIESSL v. MAYENDORF. "Ein Beitrag zur Symptomatologie der Tumoren des rechten vorderen Schläfenlappens," *Jahrbuch f. Psychiatrie*, 1905, **26**, 13.

[15] OPPENHEIM, O. "Die Geschwülste des Gehirns," Wien, 1896, p. 219.

[16] PATON, L. "Optic Neuritis in Cerebral Tumours," *Trans. Ophth. Soc. U. Kingdom*, 1908, **28**, 121.

[17] PFEIFER, R. A. "Myelogenetisch-anatomische Untersuchungen über den zentralen Abschnitt der Schleitung," Berlin, 1925.

[18] SACHS, B. *Journ. Nerv. and Ment. Dis.*, 1911, **38**, 423.

[19] SCHWAB. "Zur Diagnose der Schläfenlappentumoren," *Deutsch. Zeitschr. d. Nervenheilk.*, 1925, **84**, 38.

[20] STEWART, T. GRAINGER. "The Diagnosis and Localization of Tumours of the Frontal Regions of the Brain," *Lancet*, 1906, **2**, 1209.

Notices of Recent Publications.

The Matrix of the Mind. By F. Wood Jones and Stanley D. Porteus. Pp. 457. Honolulu: University Press Association. 1928.

The attempt to place psychology on a more scientific basis has, during the last few years, led to the appearance of several books in which the structure of the nervous system is presented from the point of view of its evolution and function, in which, in other words, the brain is treated as the organ of mind and mental phenomena are, as far as possible, interpreted in terms of neural physiology. This excellent and interesting volume, the purpose of which is to bridge to some extent the gap between neurology and psychology, is written in a charming and lucid style, and so simply and consecutively that it will be intelligible to even those who are unfamiliar with the anatomy of the brain in the ordinary sense of the term. One author has been a well-known anatomist and is now a professor of anthropology, the other is a psychologist; their collaboration has been so intimate that it is scarcely possible to detect the sections for which either is responsible, but the first 300 pages must have come mainly from the pen of Dr. Wood Jones. After preliminary chapters on the ontogenetic development of the nervous system, the evolution of the fore-brain is traced from the first rudiment of a centralized nervous apparatus, function being as far as possible correlated with the growing complexity of structure. The nature of the pallium and its relation to more lowly placed parts are then discussed in such a manner as to bring into relief the great possibilities for further advances that the appearance of this plastic organ furnished. Chapters on the conduction and integration of sensation follow, and emphasis is particularly laid on the importance of the co-ordination of sensory impressions on the development of the cerebral cortex. The parts that the pallium and the corpus striatum take in movement and the anatomical connections that make their activity possible, are fully considered, as well as the influence on movement of the labyrinths, the cerebellum and other subcortical centres. Unfortunately the author is not conversant with much of the recent work on speech and aphasia. The second part of the book, which is written from the psychological side, emphasizes again the importance of structure in attempting to interpret function. There is here and there too facile an attempt to explain Nature's purposes and unravel all her secrets; in fact, the teleological attitude of the writer is at times wearisome, but his presentation of the subject is always stimulating and instructive. Hypotheses abound, but in most instances they serve at least to illustrate or to make intelligible more fundamental facts.

The authors have produced an extremely healthy and readable volume which will afford interest and instruction to readers of every class.

Brain and Mind, or the Nervous System of Man. By R. S. A. Berry. Pp. 608, with 130 illustrations. New York: The Macmillan Co. 1928. Price 31s. 6d.

The author is a well-known teacher of anatomy who is also interested in psychiatry, but his book is written for the psychologist, the educationist and the social worker rather than for the physician and the student of medicine. As a textbook on anatomy it is not very satisfactory and falls below the level of many others available, for though it contains few inaccuracies and, except in the case of the fore-brain, no striking omissions, its arrangement will not give the student a clear picture of the structure of the brain as a working mechanism. Most of the illustrations are borrowed from other sources and are not particularly well selected; the description of diagrammatic drawings as photomicrographs of the cortex is an unfortunate oversight in a volume intended for the uninitiated. The attempts at the interpretation of function on both the physiological and psychological sides are open to more criticism. His main thesis is that the internuncial neurons are the physical instrument of mind, but he proceeds to the crude assumption that they are the store-houses of memory, speech, reason and thought, and constantly implies that mental capacity and quality depends merely on the number of neurons, as in the use of the term "multineuronic geniuses." Conversely amentia, of which he makes only an anatomical classification, is simply due to a deficiency of neurons. Many pages are devoted to measurement of the head as an aid in the diagnosis of mental abnormality, and several tables are supplied which may be employed in correlating the measurements obtained. Criminality, prostitution and hysteria are grouped together as symptoms of a small brain. There is also a tendency to accept uncritically unproven hypotheses and to make loose statements on function, as that pain is conducted by non-myelinated fibres, that postural tone is the special property of the autonomic arc, and that tabetic ataxia is due to the cerebellum not receiving impulses from the dorsal columns. On the other hand, much of the recent work on the physiology of the nervous system has been neglected; no reference is made to Magnus's researches in the discussion of the functions of the brain-stem, or to Pavlov in describing the activity of the cerebral cortex.

Handbuch der Neurologie des Ohres. Herausgegeben von G. Alexander, O. Marburg und H. Brunner. II. Band, 1te Hälfte. S. 722, mit 155 Abbildungen. Berlin und Wien: Urban und Schwarzenberg. 1928. Price M. 75.

The first and third volumes of this encyclopædic treatise on the neurology of the ear have appeared during the last five years and have been noticed in this Journal; the second volume will deal with more special subjects, and its first half, running to 720 pages, is under review here. As the previous parts, it contains some matter which is only very indirectly connected with the

auditory or labyrinthine apparatuses: Sträusslers' long chapter on the congenital defects, malformations and heredogenerations of the nervous system may be mentioned as an example, though this is an interesting and useful compendium on the subject for the neurologist.

The first chapter, by Pollak, deals with the affections of the facial and trigeminal nerves associated with diseases of the outer and middle ear: the second, by Spiegel, with involvement of the sympathetic system. Other chapters of particular interest to the neurologist are those on deaf-mutism by Urbantschitsch; cerebral concussion and fracture of the base of the skull, by Schönbauer and Brunner; the aural symptoms in various cerebral diseases by Alexander, and the vascular affections of the brain-stem and cerebellum by Stiefler. Sections on aural concussion, gunshot wounds of the ear, injury of the ear by changes in atmospheric pressure and vascular disease of the labyrinth, will appeal more strongly to the otologist. This part maintains the same high level of subject matter, editing and production that distinguished the previous volumes.

Kehlkopf und Rachen in ihren Beziehungen zu den Erkrankungen des Zentralnervensystems. Von B. Freystadtl. S. 324. Berlin: S. Karger. 1928. Price M. 17.

This textbook deals with the functional disturbances of nervous origin of the larynx, pharynx and tongue, as well as with the disorders of deglutition, respiration and articulation, that result from interference with their nervous control. In the first section the anatomy and physiology of these structures is discussed in considerable detail, and the symptoms that result from lesions of the different motor and sensory nerves that innervate them are described. This section is on the whole satisfactory, but it would have been more readable and useful if the author had been content to state his own experiences, or had collated them briefly with the views of others, but an uncritical collection of all manner of hypotheses is the usual failing of almost all such compilations. The second and larger part of the book is devoted to a description of the pharyngeal and laryngeal symptoms that form part of, or may occur in, different nervous diseases. A bibliography at the end of the book may be useful to anyone who wishes to find references to rarer laryngeal symptoms of nervous origin.

Experimentelle Neurologie (Physiologie und Pathologie des Nervensystems). By E. A. Spiegel. S. 281. Berlin: Karger. 1928. Price 24 M.

This volume constitutes the first part of a treatise on experimental neurology, the second half of which is due shortly to appear. While there is no lack of excellent monographs dealing with the morphology of the nervous system, there is an obvious need for a modern and comprehensive textbook dealing more particularly with the physiological aspects. Dr. Spiegel's book

admirably fills this gap. In this first volume he deals with the methods of investigation which lie at our disposal; then follows a general consideration of the nature of the nerve impulse. The beginner is recommended to commence the work by reading Chapter III, which deals with the reflex activity of the central nervous system. Chapters on the segmentation of the spinal cord and its roots, and on the vegetative nervous system, complete the volume. The work is illustrated by original diagrams which are lucid and admirably drawn.

We are promised in the second volume a consideration of static and kinetic innervation, of the course of the centripetal nerve impulse, the physiology of consciousness, the circulation of blood and spinal fluid and lastly a bibliography. When completed, Dr. Spiegel's work will constitute the most important monograph of its kind.

Handbuch der biologischen Arbeitsmethoden. Abt. 5. *Methoden zum Studium der Funktionen der einzelnen Organe des tierischen Organismus.* Teil 5a, Heft 4. By URBAN and SCHWARZENBERG. Berlin and Vienna. 1928. Rm. 8.

This volume is a recent contribution to the exhaustive textbook on the methods of biological research which is in the course of publication under the editorship of Professor Emil Abderhalden. The following papers are contained in this particular number: "The Theoretical Basis of the Methods of Estimating the Elastic Properties of Muscle," by Steinhausen; "The Rate of Course of the Wave of Contraction in Muscle and the Speed of the Nerve Impulse," by Schiff; "Methods of Estimating the Latent Period in Muscle," by Schiff; "Kymocyclographic Methods of Investigating Movement," by Bernstein; "The Illustration of the Nerve Impulse by Means of Models," by Ebbecke. Research workers in the domain of muscle physiology will appreciate the value of these important contributions.

Organic Inheritance in Man. By F. A. E. CREW. Pp. 214. London and Edinburgh: Oliver and Boyd. 1927. Price 12s. 6d.

The subject matter of this volume is based upon the first series of William Withering Memorial Lectures delivered at the University of Birmingham. The first few chapters concern chiefly the biological and mechanistic aspects. Of particular interest to medical men are Chapters VI and VII, in which the normal and abnormal features of organic inheritance are treated. Herein the author deals in a most interesting fashion with the transmission of morphological peculiarities, and with such problems as those of sinistrality and longevity; the question of blood-groupings and their medico-legal importance in cases of disputed paternity; Manoilov's test for identification of races and twinning; these are only a few of the many problems that are considered. A special chapter is devoted to the questions of inbreeding and parental consanguinity. In the sections on the pathological aspects the various heredo-

familial affections are tabulated according to their biological characteristics—whether dominant or recessive. One may quote some of the author's practical suggestions as to a policy with regard to imbecility; the feeble-minded should not be allowed to marry into a family in which there is a history of feeble-mindedness; paupers, criminals, habitual drunkards, vagrants, prostitutes, should be examined carefully and scientifically in order that the victims of circumstance might be separated from the victims of organic inheritance and treated differently; the feeble-minded should be segregated. The author suggests that sterilization should be considered, but he points out that libido is not extinguished by this means, and hence the spread of venereal disease still remains a possibility. In the appendix there are numerous genealogical tables illustrating the mode of inheritance of various diseases, including many neurological disorders.

Dr. Crew's monograph can be recommended as a most valuable and instructive account of a difficult but fascinating aspect of medicine.

The Opium Problem. By CHARLES E. TERRY and MILDRED PELLENS. Bureau of Social Hygiene. Pp. 1,042. New York. 1928.

This detailed and comprehensive study of the problems of morphism in all its aspects was drawn up as a report presented to the Committee on Drug Addictions. Questions of ætiology, symptomatology, withdrawal phenomena and treatment are dealt with in turn. The latter half of the volume concerns the sociological, national, state and municipal efforts at legislative control of the opium traffic. All who are interested in any aspect of morphism will find in this encyclopædic report a wealth of data, enhanced by quotations from other workers in this field. A very full bibliography completes the volume. One will not find, however, any dogmatic conclusions based upon personal experience, for the report is essentially a compilation. Such expressions of opinion as are found are purely tentative; the factors of ætiology are regarded as inconclusive, and the authors indicate the need of a carefully conducted study covering a long series of cases. With regard to the social and psychical status of the *habitués*, we read that opium addiction is not restricted to any social, economic, mental or other group; that there is "no type which may be called the habitual user of opium, but that all types are actually or potentially users." Speaking of treatment, the authors stress the ambiguous significance of the word "cure," and they restrict this term to the return of the patient to somatic and psychical integrity. Most of our therapeutic measures have not advanced beyond the stage of empiricism, and the authors deem it more desirable "to employ tentatively methods of treatment that appear to be based on such pathologic changes as are at present recognized in individual cases."

In this report we realize clearly the difficulties which have accumulated around the problem of opium addiction as the result of personal bias, the want of accurate data, and the vague impressions derived from a limited experience.

To the students of drug addiction this volume represents the most exhaustive and up-to-date *exposé* of the opium problem, and will rank with the monographs of Maier on "Cocainismus," and Beringer on "Mescalism."

Langages neologiques et des Idées délirantes en Médecine mentale. By Dr. G. TEULIÉ. Pp. 165. Paris: Auguste Picard. 1928. Price 25 frs.

This volume is an examination of the neologisms found in the language of the insane. The object of the study was to establish whether neologisms can ever reach the stage of development into a new language, and to determine the relation, if any, between such nelogisms and the ideas of the delirious flight of mania. The author, as a result of his study, concludes that neologisms and neologistic language are but degrees of one process, and that a new language in the true sense never arises in a mind with deteriorated powers. The poet and mystic alone are able to create new linguistic and coherent forms. The author attempts to give prognostic significance to the appearance and chronicity of neologisms and glossolalia, and attempts a classification. This monograph should prove of value to all who are students of the enigma of schizophrenia, but from the point of view of the study of language the material needs examining in the light of general philology. Interesting discoveries might be made.

Cours de Psychologie. By MARCEL FOUCAULE. *Tome II. "Les sensations élémentaires."* Pp. 260. Paris: Felix Alcan. 1928. Price 20 frs.

This volume is a compilation of all the data relating to the physiology and psychology of the senses. Each sense is carefully dealt with in its physical and mental aspects, and the data gleaned from pathological states receives some attention. On the other hand, the proprioceptive system receives little or no attention, and in the chapter on sensation related to movements of the head no reference whatsoever is made to the work of Magnus and de Kleijn. This volume should prove of use to neurologists who are engaged on the careful exploration of disturbances of sensibility. Ordinary neurological textbooks are poor in such information, and it calls for laborious hunting in psychological journals to obtain all the facts which the author has here gathered together.

Stammering. A Psycho-analytic Study. By ISADOR CORIAT. Nervous and Mental Disease Monographs. No. 47. Price $2.50.

This interesting and provocative monograph is frankly psycho-analytic, but it is none the less an interesting contribution to the problem of stammering.

On the basis of the psycho-analytic investigation of a series of cases, the author suggests not merely the causes of the disability, but the type of personality which is to be found amongst stammerers. He states that the

stammer arises at what psycho-analytic workers call the oral phase of development, that is to say, the subject's hedonic or pleasure interest is centred upon the oral zone of erotic interest which finds its satisfaction at the breast of the mother and in all processes related to the sucking reflex. Later the biting reflex grows out of this, and the pleasures of sucking and biting become interwoven. Frustration of the interest gives rise to negative attitudes towards the pleasure-producing object, the mother, and biting or aggression grows to represent the indignation felt as result of the frustration. The all-pervading pleasure experienced at the breast or oral stage gives rise to a feeling of complete satisfaction and dependence which, with the development of the personality, produces anomalies in character. If these views were expressed in terms of the conditioned reflex physiology, rather than in the picturesque and anthromorphic language of psycho-analysis, the theory put forward would receive wider assent and more scientific criticism.

Elementary Conditions of Human Variability. By RAYMOND DODGE. Pp. 107. Columbia University Press. Publication 10. Price $1.50.

As regards human behaviour there are two kinds of variability: personal differences in response to identical stimuli, and individual variations in response to the same stimulus. After an extensive statistical investigation of stimulus and type of response, a series of correlations are drawn up. The most important condition is the refractory period which limits the frequency of response when stimulation is repeated above a certain critical rate, modifies the pattern of response to repeated stimuli, and facilitates the consolidation of isolated conscious events into series. Habituation varies according to the level; the knee-jerk suffers no modification over long periods of time, although there was a gradual increase in the latent period, but on the cortical level there is a decrease of latency with habituation, which is important for the study of learning processes. Rhythmic effects were noted. All neuromuscular reactions appear to be most effective in the morning, less so in the evening, irrespective of fatigue. The value of these studies for objective psychology and its industrial and eductional applications is obvious.

Common Principles in Psychology and Physiology. By JOHN T. MACCURDY. Camb. Univ. Press. 1928. Pp. 280. Price 15s. net.

If there is virtue in conciliation, Dr. MacCurdy deserves well of both neurologists and psychologists in presenting this thorough discussion of the common principles underlying psychology and physiology. The battle between them has been as acrimonious as any scholastic debate between the protagonists of materialism and idealism, and in entering the no-man's land between the two opposing opinions he runs the risk of being sniped by the irreconcilables of both sides. In his discussion, however, the author keeps a firm foothold

in both camps, and exhibits a full appreciation of the advances made on both sides to solve the most fundamental problems of organic life. In the attempt to bring the apparent opposites together, he suggests a vocabulary which should become the nucleus of a common language. He sees in the Pattern Theory of physical and psychial processes a common ground for discussion. There is nothing new in the approach; we are conversant with it from the writings of Semon, and no one finds it difficult to apply it diagrammatically at least to the physiology of Pavlov and Sherrington on the one hand, or the Gestalt theory on the other. Where the phenomena of memory are concerned, however, as in the data of psychopathology, a pattern theory alone does not carry us very far. Conscious of this difficulty, the author turns back to the central problem of psychology—the nature of images. He argues, in dealing with Köhler's work on the mentality of apes, that some image function is at work to give rise to the successes following on trial and error. Only in conscious awareness can experience grow, and the awareness is carried over in mental growth through the agency of image functions. This view has, of course, been discussed from another angle by both Lloyd Morgan and Stout, under the form of "prospective reference," but where the author elaborates the thesis is in co-ordinating it with that linking conception—the pattern theory. This enables him to pass over to purely physiological fields. It is, perhaps, a little surprising that the data of embryology can explain themselves without reference to consciousness. Our knowledge of biochemical process has sufficiently advanced to permit us to understand "rudimentary memory" in a biochemical sense, and for all working purposes a behaviourist methodology still carries us along. It is only in a philosophic sense that the problem of consciousness arises. For scientific purposes the language of neurology and psychology will have to remain apart.

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EDITOR.